“EFFECT OF PRE-TERM BIRTH ON INTELLECTUAL ABILITY – A COMMUNITY BASED NON- CONCURRENT COHORT STUDY IN SOUTH INDIA”

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CERTIFICATE

This is to certify that "EFFECT OF PRETERM BIRTH ON INTELLECTUAL ABILITY – A COMMUNITY BASED NON-CONCURRENT COHORT STUDY IN SOUTH INDIA" is a bona fide work of Dr Chella Sindhu KN in partial fulfilment of the requirements for the MD Community Medicine examination (Branch – XV) of the Tamil Nadu Dr M.G.R. Medical University, Chennai, to be held in April, 2015

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"Three things cannot be long hidden: the Sun, the Moon and the truth"

-Lord Buddha

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Glossary of Abbreviations

AAMR – American Association on Mental Retardation

ADHD – Attention Deficit Hyperkinetic Disorder

APGAR – Appearance Pulse Grimace Activity Respiration

BIDS – Brief Intellectual Disability Scale

BKT – Binet-Kamat Test

BMI – Body Mass Index

CAP – Child and Adolescent Psychiatry

CBC – Child Behaviour Checklist

CHAD – Community Health and Development

CMC – Christian Medical College

GDM – Gestational Diabetes Mellitus

GVMCH – Government Vellore Medical College and Hospital

HA – Health Aide

IQ – Intelligent Quotient

LSCS – Lower Segment Caesarean Section

MAC – Mid Arm Circumference

MPHW (F) – Male Peripheral Health Worker (Female)

PCV – Packed Cell Volume

PHC – Primary Health Centre

PHN – Peripheral Health Nurse

PTCHW – Part Time Community Health Worker

SD – Standard Deviation

SES – Socio Economic Status

SEAR – South East Asian Region

SPSS – Statistical Package for Social Sciences

WHO – World Health Organisation

Title of the abstract: "EFFECT OF PRE-TERM BIRTH ON INTELLECTUAL ABILITY– A COMMUNITY BASED NON- CONCURRENT COHORT STUDY IN SOUTH INDIA"

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Objectives:

a. To estimate the magnitude of intellectual disability in preterm and term born children.

b. To study the effect of preterm birth on intellectual disability.

c. To study the effect of socio-demographic and medical risk factors on intellectual disability

Methods: The study design was a non-concurrent cohort study. It compared the intellectual ability of Pre-term children born between 2001 to 2005 with their Term counterparts born in the same period. The sample size calculated was 200 preterm born children and 200 term born children. An interview was conducted with the parent or the primary caregiver. Basic socio-demographic data was collected. Antenatal, natal and postnatal details were obtained. Anthropometric measurement was obtained. The screening tool (Brief Intellectual Disability Scale – BIDS) was administered by a single interviewer. BIDS (Brief Intellectual Disability Scale) score >5 is said to be screen positive for intellectual disability with a sensitivity of 71.53% and a specificity of 80.95%. BIDS (Brief Intellectual Disability Scale) score > 11 is said to be diagnostic for intellectual disability with a sensitivity of 54.29% and a specificity

of 100.00%. The BIDS questionnaire had a total of ten questions. The responses to the BIDS questionnaire was recorded in the form of Likert scale as “Not true”, “Sometimes true” or “Very true” for the all the children born by preterm and term birth by the parent or the primary caregiver.

Results: The incidence of intellectual disability among the preterm children born in Kaniyambadi block was 5.4% compared to 0.49% among the term born children. Preterm born children had 11 times greater risk of developing intellectual disability in comparison to the term born children. 59 (29.2%) of the children born by preterm birth developed probable intellectual disability (BIDS score greater than 5) compared to 11 (5.4%) of their term counterparts. Children born preterm had 6.732 times greater risk of developing probable intellectual disability compared to the children born term.

1. Introduction

Children born preterm have faced problems, beginning with a reduced survival and among survivors, a plethora of problems as a result of insults which are either direct or indirect consequences of preterm birth. The survival of preterm children has dramatically improved over the last few years with advances in medical technology.(1) On one hand we have managed to increase the survival of preterm born children by harnessing modern technology. On the other hand, despite their increased survival, these children tend to have physical, intellectual or behavioural disabilities. The intellectual disabilities include deficits in learning ability, thinking, verbal capacity, memory, behavioural problems etc.(2)

The human brain is susceptible to the various events and insults that are very often the sequelae of preterm birth. The reorganization of the brain following intrauterine growth is thereby affected following these insults. Studies have shown that the cortical volume, thalamic arrangement, neuronal reorganization, white matter microstructure and the folding of the cortex are negatively influenced by prematurity and its effects.(3)(4)

It has been believed for a very long time that intellectual outcome for babies born preterm does not differ substantially from those born at term. However, prospective studies conducted over the last few years have however highlighted the poor outcomes in cognitive, behavioural and educational functions in the preterm born infants. There is very little evidence at present to substantiate this completely but studies do indicate subsequent effects especially with respect to cognition.(5)

Among the preterm born infants, a few children do harbour minor deficits which do not grossly affect their intellectual functions. However the more unfortunate tend to face

significant problems in the domains of learning, behaviour and emotions. This vulnerability among these children is due to multiple causes and reasons. The socioeconomic status, parenting quality, quality of life, genetic factors, severity of the brain injury, environmental factors and broncho-pulmonary dysplasia may also influence the already established intellectual deficit apart from the inbuilt intrinsic factors and the preterm insults encountered before and during birth.(2)

If some of these factors are predicted at an early stage of development of the child, it will be easy to identify intellectual disabilities. It can initiate early interventions to initiate the necessary modifications in the upbringing up of such children. These children, without these interventions may face challenges well beyond their capacity. These challenges in turn may have detrimental effects on their personality and behaviour and affect family harmony. These interventions could reduce the impairment to a level that is not a major impediment for the child to lead a reasonably normal productive and an independent life.

Many methods have been evolved over the course of time to improve the care of children with intellectual problems. Adapting the environment to the child's need and enabling the parents or the caretakers to understand the ability of their own child and adjust accordingly might to a large extent mitigate the developmental and cognitive problems to a very great extent.(6)

Children who grow up in congenial, stable and affluent family environments tend to perform well in intellectual tests than their counterparts from less stable family environments and low income groups. Hence environments both at home as well as in the society definitely have a strong impact on the possibility of coping with the intellectual problems that a child may have as a consequence of premature birth.(7) (8)

Many studies have been done by following up the national registries to evaluate the outcome of preterm birth on the development and survival of the various cohorts of children. A study done on the Norwegian birth registry in 2008 identified 2805 infants born at 28 to 30 weeks and 7424 at 31 to 33 weeks, 32,945 at 34 to 36 weeks respectively. The study demonstrated an increased risk of cerebral palsy (RR= 78.9), mental retardation (RR= 10.3) and of getting disability pension (RR=7.5) among those born between 23 to 27 weeks. (9) A Swedish study concluded that the infants born at 33 – 36 weeks of gestation showed higher odds of getting long term intellectual impairment.(10) A direct association between cognitive level and gestational age was shown by another study from Sweden published in 2010.(11) This study showed a stepwise decrease in cognition with decreasing gestational age.

Another study on preterm cohorts in Sweden has shown that there is an increased incidence of a multitude of underlying psychiatric disorders.(12) A retrospective study from the United States (US) in 2009, conducted on 1,41,321 children showed that infants born at 34 weeks of gestation had a hazard ratio of 3.39 and 1.25 for cerebral palsy and mental retardation respectively. The study concluded that preterm birth is linked to negative effects in neuro-developmental sequelae.(13) A recent study from the United States found that prematurity and low birth weight are critical risk factors for neuro-developmental problems and mental health diseases.(14)

The current estimate of premature births is at the rate of more than 1 in every ten births worldwide. This amounts to a total of around 15 million babies born preterm every year. Around 1.1 million of these children die and the rest live with disability which are often unidentified and unaddressed to.(15) In the South East Asian region (SEAR), the WHO (World Health Organization) has attributed preterm birth as the cause of neonatal death in

30% of cases. In a study from India it was found that preterm birth was the leading cause of neonatal death at an alarming rate of 27%.(16)

A prospective cohort study from Pune, Maharashtra demonstrated that children born preterm, who are small-for-gestational age, had the worst cognitive ability.(8) Other than the above mentioned study, there is scarce literature from India regarding the cognition and development of intellect among preterm born children. This scarce literature and evidence is especially critical in a country like India that tops in the number of pre-term babies delivered every year.(16)

Identifying the learning and cognitive impairment in these children will play a pivotal role in preventing long term disability by early diagnosis and appropriate counselling for the parents or caregivers with the necessary treatment for the child. This needs effective screening which is specific as well as cost-effective for such groups of children, especially for those born in a developing country like India. (10)

2. Justification

India has the largest number of premature births in the world.(17) It therefore is prudent to look at the incidence and the effects of serious intellectual disability and impairment among the preterm births. It is also necessary to look into the various risk factors that are causative for intellectual disability in the process of preterm birth and to pragmatically look for approaches to reduce some of the major risk factors leading to preterm birth and thereby its sequelae with complications, the predominant one being defects in cognition.

A majority of the risk factors and complications associated with preterm birth are still under study. Data on preterm birth and its associated complications later in life are still scarce, especially in the developing world, more so when the factors leading to preterm birth might be somewhat different in the developing world when compared to the developed world.

By early detection and thereby incorporating the relevant changes in the care of such children, major adversities in their growth and development can be avoided reducing the morbidity and challenges that these children face.

The Pune low birth weight study clearly showed that the preterm small for gestation age children constituted the major proportion among those children who had problems in cognition.(18) Hence extra care is to be rendered to this particular section of children right from an early stage.

Children need to be taken care of very specially and need to be provided with healthy environmental conditions more so for children with cognitive and intellectual deficits where they generally grow up in a hostile and a demanding environment especially with respect to academic performance. Unidentified disabilities in children can add to the

morbidity related to child's development and this can add to the stress in uninformed and inadequately prepared parents. This can indirectly affect the growth of a society and the nation, which is dependent on its physically and mentally healthy children. There is therefore a definite need for appropriate and cost effective methods to identify children at risk of intellectual disabilities and incorporate the necessary correctional measures and modifications at crucial points of time that are needed to make them grow into a reasonably normal child with no major impairments to lead at least a moderately productive independent life.

There is need to identify and enumerate children with intellectual disability to plan further remedial measures, and essential early remedial measures are to be incorporated for anticipated intellectual and cognitive deficits among those born preterm. Hence this study (EPIAS – Effect of Pre-term birth on Intellectual Ability, South India) is vital, primarily based on the magnitude of the prematurity in our nation and the meagre data available currently on intellectual disability among preterm infants. It is also necessary to identify a screening tool that can be used effectively at a low cost.

The current study (EPIAS study) aims at identifying pre-term births in the birth cohort between the years 2001 to 2005 in Kaniyambadi block and screen the children for Intellectual Disability using Brief Intellectual Disability Scale (BIDS) in the identified group of children (who are now in the age-group of 8 to 13 years). Term born infants from the same birth cohort will also be screened for Intellectual Disability using Brief Intellectual Disability Scale (BIDS). BIDS is very simple and easy to administer and is very suitable for areas where cost is an important concern. . The BIDS tool can be administered by an interviewer with minimal training. The tool also has a high sensitivity and specificity

After screening the eligible children by using BIDS, children found to screen positive would be referred to Department of Child and Adolescent Psychiatry (CAP) for further evaluation for Intellectual disability. One of the important tests used there would be the Binet-Kamat Test of intelligence (BKT).

Intellectual disability can be a major stressor in the families of these children who are often expected to be competitive in academics. A tool which can effectively be used to identify intellectual disability can help in the parents' understanding their child's intellectual capacity at a very early stage of life. Early detection is beneficial at a stage where the child has not yet made career choices. Early detection can give him or her better opportunity to choose an appropriate career for them where they can perform better according to their own intellectual ability without undue stress.

The ultimate aim is to plan a screening programme for early detection of intellectual disability for pre-term births, in a community setting where many of the preterm born children with intellectual disability go unidentified with no help or intervention of any sort both medically as well as socially. We hope that this study can provide the platform for the planning and implementation of viable screening and rehabilitation program.

3. Literature review

3.1 Preterm birth

Birth of a baby before 37 weeks of gestation in-utero is termed as preterm birth. Premature birth is the birth of a child before the developing organs are mature enough to allow post-natal survival of the baby independently.(19) Its aetiology is multi-factorial. It is difficult to deduce the incidence of this condition especially in the developing world with poor or minimal health information available. The preterm births are mostly due attributed to three main causes. They include the iatrogenic or medical reasons (25%), premature rupture of membranes (25%) and idiopathic (50%).(20) The reasons behind preterm birth are predominantly due to three main reasons. 40-45% are due to preterm labour and 25- 30% due to premature rupture of membranes and the rest are due to physician induced labour for various obstetric reasons.(21) The rates of preterm birth in Europe and developing countries in 2008 were between 5 to 9% and it was between 12 to 13 % in the United States of America.

Causes of preterm birth:

The causes of preterm birth are multi-factorial; however infection and inflammation seem to be central in the initiation of preterm labour. The causes can be divided into maternal and foetal factors.(22)

Maternal factors:

Race is a major determinant of preterm birth rates with predominant number of pre-terms born in the black race followed by the other races.(23)

Women from the Indian subcontinent have a higher chance of having a low birth weight child due to decreased foetal growth than due to prematurity. Hard physical labour and

stressful jobs increase the chance of pushing the mother into preterm labour.(24) Previous preterm delivery and a decreased gap between the pregnancies increases the risk of preterm delivery by 15% to 50%. (25) (26) A poor maternal nutritional status is an independent risk factor for preterm delivery. (27) Clinical depression and social stresses might compound the other risk factors and increases the risk of preterm births.(28) (29) Substance abuse, smoking, heavy drinking are other known risk factors for preterm labour. Intra uterine infection contributes to 25 to 40% of preterm births.(30) (31) A short cervix, cervical insufficiency, genetic causes, family history of preterm births, are also other known causes for preterm births.(32) Recent studies have shown that infection is the main cause for extremely preterm children. Lifestyle factors leading to stress are among the major causes for late preterm and moderate ones. (20) Multiple pregnancies due to assisted reproductive technology are a significant contributor for preterm births in the recent times. Single pregnancies as a result of in-vitro fertilization are also at an increased risk of preterm birth. (37)

The advantage of knowing the aetiology is that the mechanism of this condition can be elucidated and can guide future interventions to prevent the onset of preterm labour in those with these known risk factors and also stratify the risk and aid in the clinical management and preventive medicine.(21)

The vulnerability of preterm children to various medical problems:

The preterm children have poorly developed organelles, most notably poor brain and lung maturity.(33) This can grossly impact their future holistic growth. They have higher rates of hypothermia, breathing difficulties, spells of apnoea, poor glycaemic control, epilepsy, hyper-bilirubinemia, kernicterus, difficulties in nourishment, periventricular

leucomalacia, and multiple episodes of repeated hospitalizations.(34) Preterm infants also contribute to a significant proportion of infant deaths.

Very preterm births:

There has been a great change in the resuscitation of very preterm babies with the advent of assisted ventilation, surfactant therapy, antenatal steroids and change in the philosophy of resuscitation which has lead to larger number of survivors before 28 weeks of gestation.(35) However, selective management of children who have a huge chance of surviving, has led to an increase of cerebral palsy at an estimate of 7.2 per 100.(36) The survival of these children born very pre-term depends largely on the level of care received by these children during the neonatal period.

3.2 Classification of Preterm births

Prematurity or Preterm birth is further classified based on the gestational age in to four categories. They include:

- Extremely preterm (<28 weeks)
- Severe preterm (28-31 weeks)
- Moderate preterm (32-33 weeks)
- Late preterm (34-36 weeks) (21)

Since birth weight is easier to measure than gestational age it can be used as a surrogate for assessing the premature birth rate.

Low birth weight is classified as:

- Low birth weight (Less than 2500 gram)
- Very low birth weight (Less than 1500 gram)
- Extremely low birth weight (Less than 1000 gram)

Of the children whose birth weights were less than 2500 gm at birth, one third were preterm. Of these low birth weight infants , those with very low birth weight and extremely low birth weight contributed to the majority of the children born preterm.(38)

The 2007 estimate for the neonatal care in United States ran up to $26 billion. But the true cost may amount to even $50 billion. If the post-natal morbidly is also included the total expenses would be even higher. (39)

There is a direct relationship between the duration of gestation and the survival of the child. Shorter the duration of gestation, higher is the chance of morbidity and mortality due to prematurity. Most of the premature infants have the highest risk of death in the first year of life that too, in the first month of their life - the neonatal period which is the most crucial period.(40)

3.3 Complications in children born preterm

Preterm children are at risk of many major complications. Those born before 32 weeks of gestation are prone to intra-ventricular haemorrhage.(41) The major central nervous system consequences include cerebral palsy, retinopathy of prematurity, hypoxic ischemic encephalopathy and developmental delay. Since the thyroid gland is immature in a preterm child, the depletion of maternal hormones leads to neuro-developmental sequelae unless supplemented earlier.(42)

Preterm children have an immense burden of critical cortical connectivity problems.(43) They tend to lack the essential connections between the frontal and occipital lobes which is critical for the learning pattern of language. Hence they encounter learning and cognitive disabilities.(44)

3.4 Prognosis

Though children adjust well at childhood and adolescence, the chances of disability are higher near the limits of viability.(36) In a follow-up study on extremely premature children it was found that 46% had severe disabilities like cerebral palsy, visual or hearing loss and learning disabilities. 34 % had mild disabilities, 20% had no disabilities and 12% had disabling cerebral palsy. (9)

With the improvement in the survival, there has been a paradigm shift in the focus towards prevention and reduction of long term disabilities in preterm children.(45) This is particularly with respect to those related to the neurological complications. There is an inverse relation between the level of educational achievement and the gestational age.(46) The extremely premature children have an increased risk of medical and social disabilities which carry on to adulthood.(45) These disabilities include the social and emotional disabilities, disorders of psychological development, behavioural problems, epilepsy, hearing and visual disabilities, cerebral palsy, intellectual disabilities. These children born preterm are prone to depression and poor myelinisation of the executive domain and frontal lobe. They are liable to be dependant throughout their life.(47)

3.5 Low birth weight

Many preterm children have low birth weight too. Low birth weight also affects the neuro-developmental progress of a child. It has been proved that the major part of the

human brain growth occurs from mid pregnancy till the late infancy. If the brain growth does not catch up in the low birth weight children before 8 months of their corrected age then it has a negative impact on the neuro-developmental progress of the child.(48) Very low birth weight children who are mostly born preterm are prone to have low IQ (Intelligence Quotient) scores.(49) These low birth weight children also have learning difficulties in reading, mathematics, spelling, receptive language and speech.(50) They also tend to have visual motor dysfunction and are hyperactive than their peers.(51)

If there is a catch up growth within one year of age the outcomes are better as shown by Tudehope et al.(52) The neurological insult can be prevented only by avoiding the nutritional and hypoxic ischemic insult of the child during birth and post natal period. The environmental factors at home do contribute significantly to the growth of the child after discharge from the hospital.(53)

3.6 Magnitude of the problem

Every year 15 million children are born preterm as per the WHO estimate. About a million babies die of prematurity. Preterm birth is the major contributor towards neonatal deaths world over.(17) In 2005 the estimated cost of medical and educational expenditure and loss of productivity amounted to more than 26.2 billion US dollars.(17) With 14.9 million preterm births worldwide, the preterm birth contributes to a birth rate of 11.1% over the total 135 million live births worldwide in 2010.(54)

3.7 Preterm birth scenario in the developed and developing world

There has been a drastic rise in the rate of preterm birth in the developed nations over the past 20 years. The incidence is 9% in developed nations according to the 2012 WHO reports.(55) In the developing world over 60% of preterm births occur in Africa and south

Asia. Within the developing countries, the poorer the socioeconomic status, higher is the risk of premature birth.(17) Ten countries with the highest rates of preterm birth per 100 live births fall in the sub-Saharan area except two countries. However India tops the list in the highest number of preterm children born in any country which is alarming.(17)

3.8 India

India has shown a rising trend in the number of premature births with 23.6% of the global burden from our country. There is no data available on the impact of preterm birth on the intellectual ability of these children. Though India is the leading in the total number of preterm births we do not have a credible data on the morbidity accountable due to preterm birth. Such a data can go a long way in helping the health authorities in planning and implementing the appropriate measures to curtail the severity of such morbidities.

Preterm birth according to the WHO criteria is defined as those children born alive before the completion of 37 weeks of gestation. They are further classified based on the gestation period as extremely preterm (<28weeks), very preterm (28 to < 32 weeks) and moderately term (32 to 37 weeks).(17)

Among preterm births, those who survive, face a multitude of problems as they grow up leading to disability. The domains include cerebral palsy, mental retardation, seizure disorders, visual, and hearing and neurodevelopment dysfunctions. The incidence of these major problems has come down considerably.(56) However it has been shown that these children without major disabilities develop understated problems in their cognitive and behavioural domains.(56) The problems include academic underachievement, behavioural problems, emotional disturbances, attention deficits, hyperactivity, poor academic performance, learning difficulties, decreased intelligence quotient, low working memory

capacity, minor neuro-motor dysfunctions, and problems in developmental coordination disorders.(39)(56)(57).

With the advent of neonatal medicine and advances in neonatal intensive care facilities many preterm born children easily survive the early days of life and enter the adulthood.(56) Even though the mortality has come down for preterm births, preterm birth is still the leading cause of neonatal deaths the world over according to the WHO fact sheet. India is the leading contributor in the world for the preterm births with 35,19,100 preterm births per year.(17)

Preterm children are more likely to have higher risk of lower intelligence quotient, academic under achievement, greater difficulties in attending regular schools and hence need more assistance for education to perform at par with their term born peers.(39)

It is construed that preterm infants have higher risk of adverse neurological outcome. But these outcomes may be seen in normal term infants too but the chances of getting the same are higher for preterm infants.(39) The environmental factors too contribute to the neuro-developmental progress of the child. This has been a major confounder in the analysis of the outcomes of preterm birth in children.(39)

3.9 Epidemiology of preterm birth

Preterm birth is the leading direct cause of neonatal deaths responsible for 35% of the total 3.1 million deaths a year the world wide.(58) It also leads to long term loss of valuable human potential among the survivors. Preterm birth is the second most common cause of death in the under five year bracket after pneumonia.

In addition to mortality, the other major problem with preterm birth is the morbidity associated with cerebral palsy, learning impairment, visual handicap, and long term physical health problem with a higher susceptibility to non communicable diseases.(54)

Neuro-developmental sequelae:

Developmental delay is a known consequence of premature birth. About a quarter of the survivors of preterm birth suffer from neurological morbidity. Cerebral palsy is often used as a surrogate marker of neonatal care. Neurosensory disability is a known problem with preterm children.(59) The advances in neonatal care and the reduction in neonatal mortality will result in a proportionate and absolute increase in the number of cases with cerebral palsy. It has been noted that preterm children tend to have minor neuromotor dysfunction and poor coordination.(60) Extremely preterm infants without cerebral palsy and with normal intelligence can have gross and fine motor disabilities.(61)

Follow up of very low birth weight infants who are mostly preterm have shown that they tend to live with cognitive deficits, poor scholastic performance, grade failures, academic under achievements and need remedial measures.(62) It has been well known that the prevalence and severity of these cognitive issues are inversely proportional to the birth weight of the baby. The difficulties in school increase with the decrease in the birth weight as shown by Saigal et al.(63) This has been noted even in preterm children who have normal intelligence and without any neurosensory impairment. Boys have a higher incidence of learning difficulties than girls.(63)

Behavioural sequelae:

Very preterm infants have high rates of dysfunction in attention and visual processing. They tend to perform lower than term children in reading, spelling and mathematics.

These cognitive deficits tend to persist into late adolescence and early adulthood too.(64) However environmental modifiers like parental socioeconomic status, parental education, two parent family, racial origin, neighbourhood factors, education, influence the severity of cognitive impairment.(65)

There is a fourfold risk of attention deficit hyperactivity disorder in very preterm children. Emotional problems tend to affect the schooling and learning of these children.(66) There is a reported higher prevalence of anxiety and depression among the survivors of preterm birth.(67) However risk seeking behaviour and delinquency are lower than their normal counterparts. Though the preterm cohorts tend to fare poorly in academic achievement, employment and ability to lead an independent life, long term studies have shown that in adult hood they tend to adapt well in to their social role and perform better than what was expected out of them.(18) (68)

Other sequelae:

Preterm children tend to have higher rates of hospital visits and hospitalization in their first two years of life mostly due to respiratory illness.(69) (70) In the later ages it is mostly for physiotherapy or occupational therapy. The preterm children tend to have growth retardation in the initial years and catch up as they grow, with increase in their body mass index to levels which risk them to cardiovascular and diabetic disorders.(71) They tend to have high blood pressure. Other health issues noted among the preterm children include broncho-pulmonary dysplasia (72), retinopathy of prematurity (73), hearing impairment, central cortical auditory processing (74) which can in turn affect the higher cognitive functional development to a significant extent.

Functional outcomes in preterm children:

Self reports by teenagers and by the parents of extremely low birth weight children showed that they tend to have greater prevalence and complexity of functional limitations than the control teenagers. They however reported a high valuation on their health related quality of life. This phenomenon of higher self rating of the quality of life is called disability paradox (75). However such self reported quality of life assessment throws light on the way people value their life and assess based on their limitations.

Impact on the family with preterm children:

A negative emotional and social impact has been shown in families with preterm children with sequelae. The greatest was during the first year of life and it persisted at a higher level than the control families. The factors influencing the impact on families include family income, parental education, and the severity of the problems in the child. After adolescence the socio economic factors does not affect the family significantly whereby an adaptation of the child to the environment occurs. They tend to have a positive feeling of mastery and accomplishment and positive interaction with friends.(76)

Influence of level of perinatal intensive care:

Saving the smallest babies is an ethical dilemma especially in the developing and poor nations. However with the advances in the level of neonatal care babies treated at level III neonatal care, fared better than those born and treated elsewhere.(36)

3.10 Long term consequences of preterm birth in children

The specific physical effects of prematurity includes visual impairment secondary to retinopathy of prematurity, hearing impairment, chronic lung disease and long term cardiovascular ill health.(77) Neuro-developmental issues include academic

underachievement, dyslexia, and specific learning impairments, moderate to severe cognitive impairment, cerebral palsy, attention deficit hyperactivity disorder, increased anxiety and depression. These problems affect the family psychologically, emotionally and financially. It also burdens the cost and expenditure of the health care system, and increases the risk of premature delivery in future pregnancies(54).

Worldwide, there is very minimal data on the acute morbidities and the long term impairments associated with the preterm births. It has been estimated that 43% of the surviving 0.9 million preterm babies are with neuro-developmental impairment predominantly from the middle income countries. This study will centre on the less severe disabilities and elaborate on the intellectual disabilities faced by this cohort of new born in their future.

3.11 Dexterity and motor functions

Children born preterm with normal intelligence and no cerebral palsy tend to have minor difficulties with coordination. These include fine motor, visual motor, visual perceptual, and visual spatial tasks.(39) The gross motor functions are better than the preterm children with cerebral palsy but these subtle difficulties faced by these children over a period of time lead them to disappointment affecting their self esteem and association with their peers and society. These difficulties pose a major hurdle to their mental peace and harmony leading to poor scholastic performance as well unstable personalities.

It goes a long way to identify these minor problems early in life so that the parents and teachers can be forewarned on what to expect out of the these children and chart realistic modifications in the plan for future training of these children.(39) Williams et al. had shown that motor impairment was three time higher among the preterm children than their term counterparts.(78)

3.12 Cognitive impairment

Intelligence is a composite of multiple faculties that should be properly integrated including visual perception, visuo-spatial processing, visual and auditory memory, processing of syntax, visual motor coordination, abstract reasoning and complex language processing. There are various tools to assess the Intelligence Quotient (IQ) in a child. In a younger child use of developmental quotient may be appropriate.(39)

It has been suggested that age corrected for prematurity should be taken in to consideration for the assessment of Intelligent Quotient in a preterm child. The American Association on Mental Retardation (AAMR) has defined mental retardation as "disability that originates in childhood and is characterized by significant limitations both in intellectual functioning and in adaptive behaviour, as expressed in conceptual, social, and practical adaptive skills".(79)

On the basis of a review of the published literature it becomes increasingly evident that preterm birth is associated with mental retardation and borderline intelligence.(39)(80) A Norwegian study has shown that preterm birth has a higher risk of mental retardation. The odds of mental retardation was shown to be 1.4 for those born between 32-36 weeks of gestation and 6.9 for those born before 32 weeks of gestation.(81)

Bhutta et al.(82) has shown in their meta-analysis that there is a general tendency for lower mean cognitive scores with decreasing gestational age and birth weight categories. This study analysed a total of 16 published case control series of children aged ≥5 years of age. The 1720 controls when compared with 1556 cases had significantly better scores in cognition. The mean weighted difference was 10.9 (95% CI 9.2 – 12.5).(82) Hack etal. (83) has shown that the Intelligence Quotient of children born preterm without neurological injuries improves with age, based on the mother's educational achievement.

However they have been found to have learning difficulties in school and academic problems when compared with their peers with average Intelligence Quotient range.

When adolescents and young adults were assessed for their IQ and compared with their term born counterparts it has been found that they have a definite cognitive shortcoming. Lefebvre et al. has shown that the cohort of children born with less than 1000 gm birth weight had lower verbal, performance and full scale IQ scores when compared with full term controls at 18 years of age.(84)

It has been shown in a study by Caravale et al that preterm birth is associated with certain specific cognitive processes in addition to lower cognitive scores, even if they had no evidence of brain injury. (85) The cognitive processes which were found to be affected included visual and motor integration, memory for identification and location, sustained attention and finally vocabulary and visual perception. Children born preterm and with lower birth weight with normal IQ scores are prone to have either as isolated or a combination of problems involving memory, attention, learning difficulties, spatial abilities, poor organization and planning skills.(86)

3.13 Learning difficulties

Literature has shown that there are many school and education related problems in preterm children. Attention deficits, speech delay, language problems, learning difficulties have been documented in such children. A specific learning difficulty is defined as a heterogeneous group of disorders of one or more of the basic psychological processes involved in understanding or in using the spoken or written language. This embraces a variety of disabilities like major problems with the acquirement and exercise of listening, speaking, reading, writing, reasoning, or mathematical skills.(39)

Aylward et al. had shown that there is more than threefold increase in the risk of subtle deficits in visual-motor and visual-perceptual abilities, complex language functions, academic functions like comprehension, arithmetic, spelling and symbols and concentration. (87)

A meta-analysis done in 2009 included 35 studies about the effect of preterm birth on neuro-developmental issues in children with a total of 4125 born preterm and 3197 controls born at term. The study revealed that the group of children born by preterm birth had moderate to severe deficits in attention, academic achievement , internalizing behavioural problems and poor executive functions.(56) The executive functions affected were verbal fluency, cognitive flexibility and working memory.

3.14 Conduct, communication and affect related issues

Conduct includes the behavioural problems which encompass a wide range of behavioural and self regulation issues like hyperactive behaviour, attention problems, sleep, eating, sensory sensitivity problems, and also anxiety, depression, and somatic symptoms.(88) The reported prevalence of these psychiatric disorders includes attention deficit hyperactivity disorder (7 – 23%), autism spectrum disorders (3.6 - 8%) and anxiety(9%).(89) During infancy the behavioural problems include speech and motor difficulties, irritability, constant crying and feeding difficulties, jitteriness, and hyper-reaction to noise, changes associated with posture, cleaning and bathing.(88)

Arpi et al.(88) has shown that behavioural problems start manifesting from infancy onwards with various described issues like meagre social interaction ability, emotional problems, reduced behavioural and emotional self- regulation and decreased concentration. They also found that behavioural problems occur along with disabilities in other domains like cognition, motor, language and neurology. It was also construed that

the length of hospital stay, severity of the neonatal interventions, mother-infant interaction issues all contribute to the behavioural problems. The study showed that infant behavioural problems are a predictor of future behavioural issues in childhood and adolescence.(88) Behavioural problems do relate with cognitive impairment. It has been suggested by the EPIPAGE ((Epidemiologie des Petits Ages Gestationnels) study, a French study that early screening is essential for the very low birth weight children.(90)

There has been a mixed opinion regarding the prevalence of autism in preterm birth. However recent literature shows that preterm birth had a strong association with autism spectrum disorders.(5) It has been shown that for each week of prematurity, the risk of autism increases. There was a three times higher risk of autism in children born before 27 weeks of gestation when compared to the others born later. Autism spectrum disorders are a group of conditions characterized by impairment in communication, social interaction and behavioural problems. It includes autism, pervasive developmental disorder not otherwise specified and Asperger syndrome.(5)

Bhutta et al (82) has shown that in addition to behavioural problems these children have other character issues like introversion, poor self confidence, with drawn behaviour and social skill deficit. Singh et al. has shown recently that premature children had 2.3 times higher odds of autism/ASD, 2.9 times higher odds of development delay, and 2.7 times higher odds of intellectual disability than term children.(14) There have been reports of delinquency, anxiety, depression, phobias, withdrawal from challenging tasks, social skill deficits affecting interaction with their peers, and are the targets of verbal bullying in schools.(87) Similarly adolescents who were preterm, demonstrated less risk taking behaviour and were less likely to violate societal laws.(39)

3.15 Intellectual disability

Intellectual disability is defined as sub-average intelligence and impaired adaptive functioning arising during the developmental period (<18 years).(91) The term “mental retardation” has a tremendous stigma associated with it. Hence it has been replaced by intellectual disability. Intellectual disability presents typically as language delay, cognitive skills delay and delay in adaptive behaviour. There also may be a delay in expressive or receptive language. Fine motor skills may be delayed like difficulties in self feeding, toileting and dressing up. They may have oro-motor in-coordination leading to disorganized behaviours like clumsy eating and constant drooling of saliva.(91)

Many developmental assessment tools have been made to screen the development of children periodically. These may be parent based surveys like Parents' Evaluation of Developmental Status (PEDS), Ages and Stages Questionnaires (ASQ) and Child Development Inventories (CDI) or instruments with direct observation like Bayley Infant Neuro-developmental Screener, Battelle Developmental Inventory, Early Language Milestone Scale, and Brigance Screens.(91)

To identify intellectual disability it is recommended to have an expanded scale of neuro-developmental and psychological examination. The psychological tests used commonly include the Bayley Scales of Infant Development-III, the Stanford-Binet Intelligence Scale, the Wechsler Intelligence Scale for Children-IV, the Wechsler Preschool and Primary Scale of Intelligence-Revised, and the Vineland Adaptive Behaviour Scales-II.(91)

The Wechsler intelligence scale for children assess four domains viz. working memory, processing speed, verbal comprehension, perceptual reasoning. Over all it gives two measures namely Full Scale IQ (FSIQ) and General Abilities index (GAI). The Full Scale

IQ is a composite of all the four domain scores while the General Abilities index includes scores from verbal comprehension and perceptual reasoning.(92)

The Child Behaviour Check (CBC) list is an exhaustive check list of questions which has various versions based on the age group of the child. The list is administered to a person who knows the child well which generally is the care giver or the parent or the teacher. In case of older child a self report form is also available where the child can fill the form on his or her own. The check list has 100 items for small children and 120 items for older children. The scores are scored over Likert scale of 0 or 1or 2 (which correspond to not true/ somewhat true/ always true). Certain questions are grouped to recognize certain syndromes. This tool helps to identify some of the commonly associated behavioural syndromes like Attention Deficit Hyperactivity Disorder (ADHD), phobias of childhood, aggressive and difficult to manage behaviours, oppositional defiant behaviours etc. The questions are then summed to scores that elicit behaviours like internalizing or externalizing behaviours and also the findings are classified ultimately as normal, borderline or clinical behaviour.(93) Hence the CBC can not only be applied to identify intellectual disability but also to elicit specific behaviours associated with intellectual compromise.

3.16 BIDS (Brief Intellectual Disability Scale)

The Department of Child and Adolescent Psychiatry of Christian medical college, Vellore has developed an abridged version of the child behaviour checklist which can be easily administered by health aids with very minimum training in a community set up where there is a dearth of physicians and a high population load. This is a shorter version of the child behaviour checklist.(94) This is the Brief Intellectual Disability Scale (BIDS). This is a ten point scale including the following questions:

- Wets himself or herself during the day
- Speech problems
- Acts too young for his or her age
- Cannot concentrate and cannot pay attention for long
- Clings to adults or too dependent on them for almost all the activities
- Gets teased a lot very often
- Does not get along with the other children
- Prefers being with younger children or those less than his or her age
- Poor schoolwork
- In coordination.

Each response is scored on a Likert scale like the CBC.

BIDS has been validated against the gold standard tests of intelligence that include the Binet- Kamat Test of intelligence (BKT), Gesell's Developmental Scheduled, Vineland Social Maturity Scale, and Attention Deficit Hyperactivity: Comprehensive Teacher Rating scale.

A score of more than 5 had an associated sensitivity of 71.4% and a specificity of 80.95% for intellectual disability. A score of more than 11 is diagnostic for intellectual disability with a sensitivity of 4.29% and a specificity of 100%.

BIDS has been found to have good inter-rate reliability and test-retest reliability with a Cronbach alpha of 0.80. There was moderate convergent validity with the Binet- Kamat Test of intelligence (BKT), Gesell's Developmental Scheduled, Vineland Social Maturity Scale and low divergent validity with the Attention Deficit Hyperactivity: Comprehensive Teacher Rating scale respectively.(94)

The test is a therefore a brief psychometric test that can be used as an easy tool to identify children with intellectual disability and is an extremely simple tool to be administered especially in the developing world comprising of both the low and middle income countries where the burden of disability strongly competes with the scarce diagnostic as well as the rehabilitative resources, both relying on an enormous finance. Also this tool can be administered by non-physicians too like health workers and paramedical staff with very minimal training.

3.17 Binet- Kamat Test of intelligence (BKT)

This is a modification of the 1934 version of the Stanford-Binet scale of Intelligence. It has been modified to suit the Indian scenario. The test harbours good internal consistency and reliability. Things like Indian coins, pictures pertaining to Indian culture and practices were incorporated to suit the Indian patient population. The areas of intelligence assessed include memory, language, thinking, reasoning, visuo-motor coordination, and social intelligence. If the IQ is less than 70 then it indicates subnormal level of intelligence as defined by Diagnostic and Statistical Manual-Version Four-Text Revision (DSM-IV-TR)(94). The main drawback of this test of intelligence is that it needs a competent professional to interpret the results of the test. The other associated drawback is the fact is that it requires an investment of at least 45 to 90 minutes per child to administer the test. At times the duration to administer the test can extend to 180 minutes especially in circumstances where the child is not cooperative. Hence the BKT is not feasible and pragmatic in an area with a high burden of preterm births.

3.18 Prevention

The parents of preterm children ought to be made aware of what to expect from their child. This will avoid the traumatic experience of knowing the deficits of their child at a

later age when not much can be instituted and thereby prevent unnecessary problems in the process of coping up of the intellectual disability of the child. It is essential to know the real incidence of the intellectual problems that preterm children would face in the future in order to be able to counsel the parents regarding the prognosis. By studying the cognitive problems in preterm children and by identifying and addressing the problem areas, possible remedial measures can be worked out. This can improve the parent child relationship and enhance the learning ability of the child who might otherwise be suffering from learning problems when left unattended, ant to thereby promote and bring about a healthy parent-child relationship and ultimately a healthy society.

4. Research Hypothesis

Children born preterm have an associated Intellectual disability which is often unidentified.

5. Aim and Objectives

Aim

To study the effect of pre-term birth on the Intellectual ability during their subsequent growth and development during childhood.

Objectives

a. To estimate the magnitude of intellectual disability in preterm and term born children.

b. To study the effect of preterm birth on intellectual disability.

c. To study the effect of socio-demographic and medical risk factors on intellectual disability

6. Methodology

6.1 Study setting

The study was conducted in Kaniyambadi block of Vellore District, Tamil Nadu. The block comprises of 82 villages with a population of 1.1 lakh and a current birth rate of 13.2 per 1000. The population of Kaniyambadi block are mainly engaged in animal husbandry, daily wage labour and agriculture and predominantly belong to the lower socio-economic status.

The Community health Department of the Christian Medical College has been working in Kaniyambadi block for the past 60 years. It provides primary and secondary health care services through CHAD (Community Health and Development) program with a special focus on Maternal and child health. It provides special care to adolescents and the elderly. CHAD has developed special programs for non-communicable diseases especially Diabetes Mellitus and hypertension. A screening program for cervical cancer is in the process of development.

A special feature of the services of the Community health department is its outreach services through mobile clinics specially established to cater to the aged with chronic diseases and provide maternal health care services to those with difficult access both geographically as well as financially to the health care centers.

The peripheral health clinics are staffed by both doctors and nurses who have been trained to work in the community. The peripheral clinic provides antenatal check-ups as well as chronic disease services. Those needing further care and evaluation or have complications are referred to CHAD hospital. Part Time Community Health Workers (PTCHWs) are trained community volunteers who have been chosen from their own community and are the first point of contact for the people from the villages. They are generally women who

have been married and staying with their family in the same village they render their service to. Each PTCHW covers a population of 1500 on an average. They keep the respective Health aide

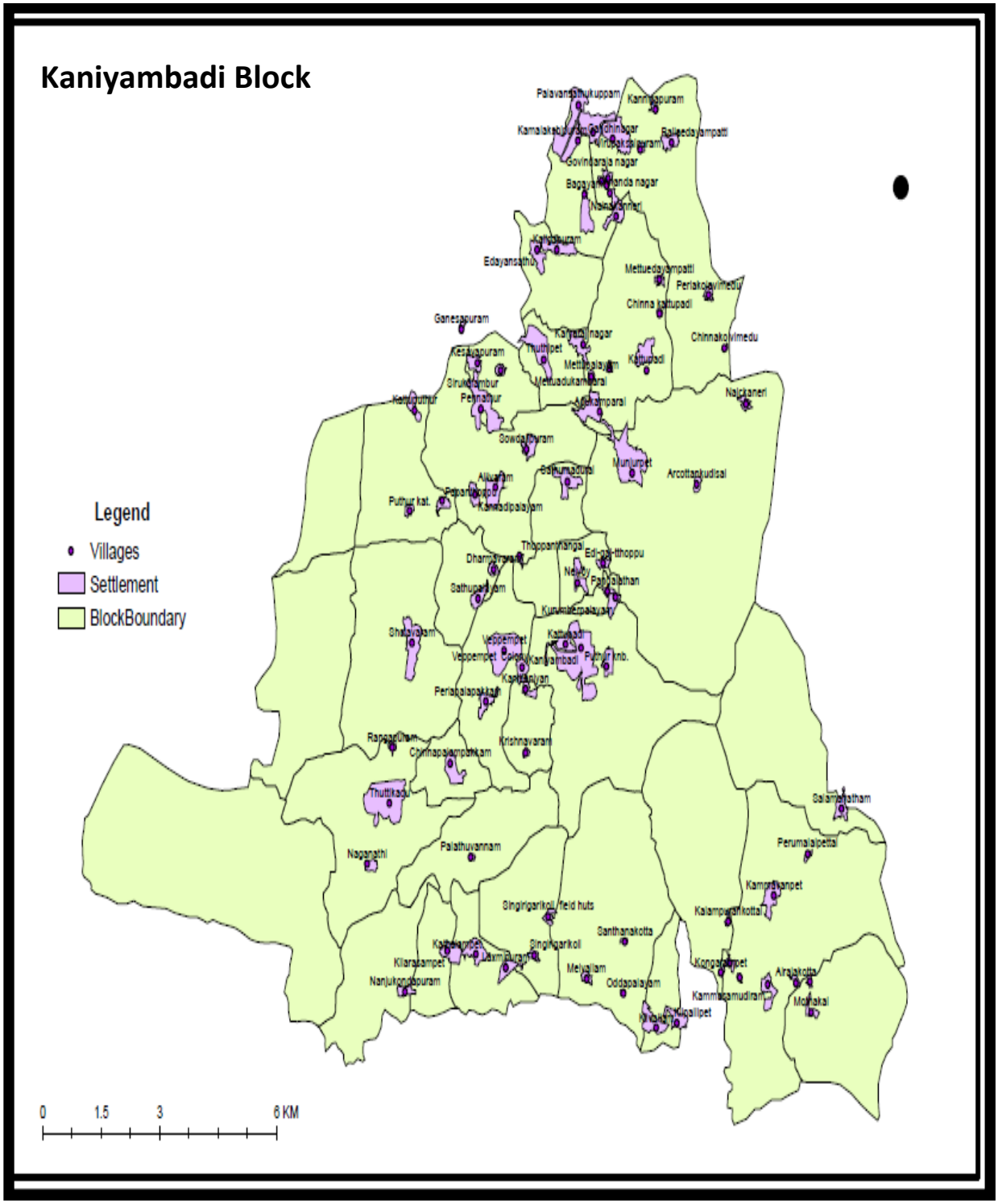


Figure 6.1 Map of Kaniyambadi block with settlement

(HA) informed about newly married couples, pregnancies, sick children and adults, deaths, and other health related issues, who in turn update this information in the Health information system (HIS)

The peripheral health clinics are staffed by both doctors and nurses who have been trained to work in the community. The peripheral clinic provides antenatal check-ups as well as chronic disease services. Those needing further care and evaluation or have complications are referred to CHAD hospital. Part Time Community Health Workers (PTCHWs) are trained community volunteers who have been chosen from their own community and are the first point of contact for the people from the villages. They are generally women who have been married and staying with their family in the same village they render their service to. Each PTCHW covers a population of 1500 on an average. They keep the respective Health aide (HA) informed about newly married couples, pregnancies, sick children and adults and deaths who in turn update this information in the Health information system.

The PTCHWs are supervised by the Health Aides (HAs) who cover a population of 5000. Health Aides are staff of Christian Medical College who reside in the same village they work in along with their family .Their job description is similar to the MPHW (F). The Health Aides are under the supervision of the Public Health Nurses (PHNs) who are graduate nurses. The PHN covers a population of 20000.

Any health related issues like births, deaths, diseases or epidemic outbreaks are brought to the notice of the doctor by the Public Health Nurse with inputs from the PTCHWs as well as the area Health aides. The peripheral health nurses are actively involved in follow-up of newborns both the healthy and the sick, post-partum mothers and the sick elderly.

The entire system is managed, co-ordinated and supervised by doctors at the Community Health Department, Christian Medical College.

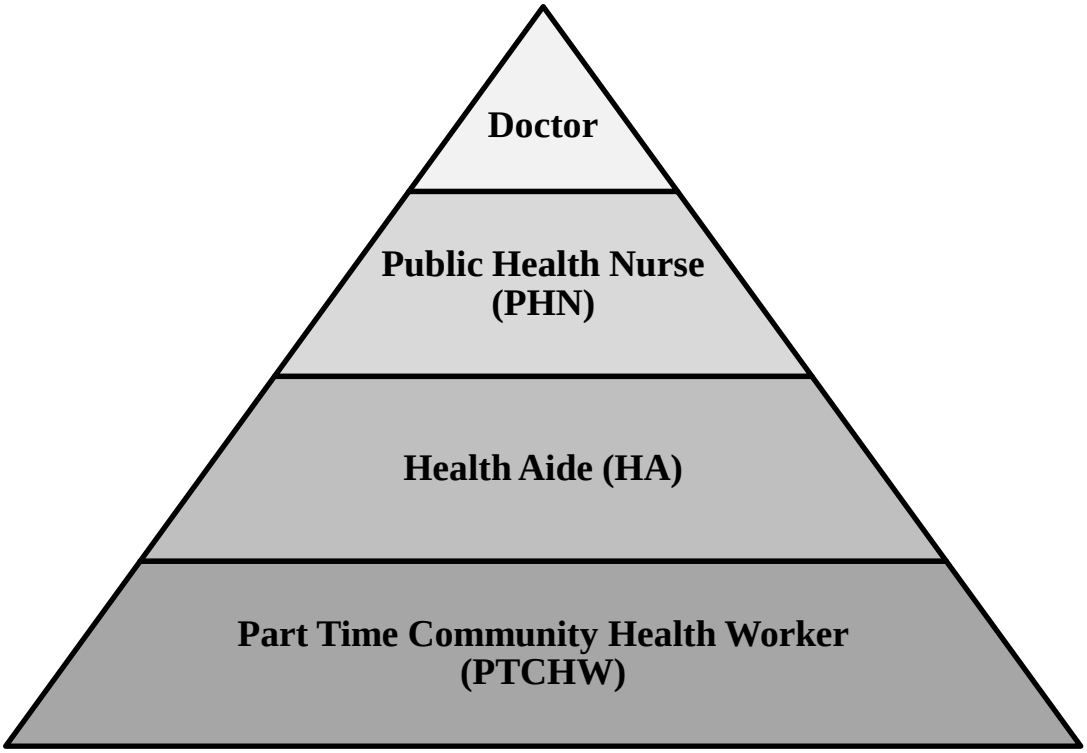


Figure 6.2 Pyramid of the health system in Kaniyambadi block

The Community Health Department has an established health information system (HIS) that records all the vital events from the Kaniyambadi block. It also records morbidity. The CHAD HIS is periodically updated by population census which is conducted once in ten years.

The various health and disease related information along with vital events is collected by the Health aides who in turn maintain records of this information in the base hospital (CHAD). These records are then verified by data mangers at the Department of Community Health and are then entered into the Health Information System.

6.2 Study population

Babies born between January 1st 2001 to December 31st 2005 were chosen as the study population. The term and Pre-term births were identified from the CHAD Health Information System. This list births was further processed to eliminate the children from the list who are currently not alive or who have moved out from the service area. The addresses of the children with street way points and street names were obtained from the CHAD database to locate the families with these children. Health Aides and PTCHWs were asked to verify the location of the families and then approached to recruit the participants into the study after obtaining an informed consent and an assent from the child.

6.3 Study design

The study design was a non-concurrent cohort study. It compared the intellectual ability of Pre-term children born between 2001 to 2005 with their Term counterparts born in the same period.

6.4 Duration of the study

The study was conducted over a period of seven months (February 2014 to September 2014). The study participants were approached mainly in the evenings on weekdays when the children would be back home from school and on weekends or public holidays ,thereby making their availability for assent as well as anthropometry possible.

6.5 Materials and methods

The study proposal was given clearance after verification by the Institutional Review Board (IRB) and ethics committee of the Christian Medical College, Vellore.

6.6 Sample size calculation

The sample size calculated was 200 preterm born children and 200 term born children.

The formula used and the calculation done is as shown:

$$n = \frac{2\ p\ q\ (Z\alpha + Z\beta)^2}{(p1 - p2)}$$

$$= \frac{2 \times 0.1 \times 0.9 \times 7.84}{(0.15 - 0.05)^2}$$

$$= 142$$

It was decided to study 200 preterm born and 200 term born children to account for the discrepancies in the gestational ages at the time of birth especially in women with irregular cycles or unknown date of the last menstrual period.

~ 200 each for exposed (preterm born) and unexposed (term born)

Total = 400

[Sample size was calculated using a prevalence of intellectual disability of 15%among the pre-term born children and a prevalence of intellectual disability of 5% among the term born children] (61)

A total of 406 children were recruited to participate in the study. Of the 406 children, 202 children were born by preterm birth and 204 children were born by term birth.

6.7 Informed consent

An informed consent (Annexure III and IV) was taken from the parent or the primary caregiver (if other than father or mother) after duly explaining in the local language about the study objectives, benefits that their children and the community on a larger scale would obtain by taking part in the study. An information sheet was also provided for future reference along with the contact details of the principal investigator. The consent was obtained either in the form of a signature or the left thumb impression in cases where the parent or the caregiver was illiterate.

6.8 Assent

An informed assent (Annexure V and VI) was obtained from the children who participated in the study after informing them in the local language. They were explained about the importance of the study and were asked about their willingness to participate in the study and thereby take part in the anthropometric measurement that included height weight and mid-arm circumference. They were allowed to discuss the same with their parent or caregiver about their preference to participate in the study.

6.9 Study procedure

Babies born between January 1st 2001 to December 31st 2005 (currently aged between 8 to 13 years) were chosen as the study population. These children were identified from the Birth register of the CHAD (Community Health and Development) program. The children who were not alive currently or had moved out from Kaniyambadi block were removed from the list. This group was chosen because their current age is ideal for the administration of the BIDS (Brief Intellectual Disability Scale) screening tool that would help in the early identification of intellectual disability. Further appropriate evaluation was done at the department of child psychiatry by referring those who were found to suffer

from intellectual disability thus giving them the advantage of early detection and appropriate therapy or management.

715 (9.46% of the total births) pre-term births and 6839 term births were identified in the birth cohort between 2001 to 2005. 42 of the preterm born children were not currently alive (5.87% of the pre-term births). Those children who were now not alive or had moved out from the study area were excluded from the list from which the sampling would be done.

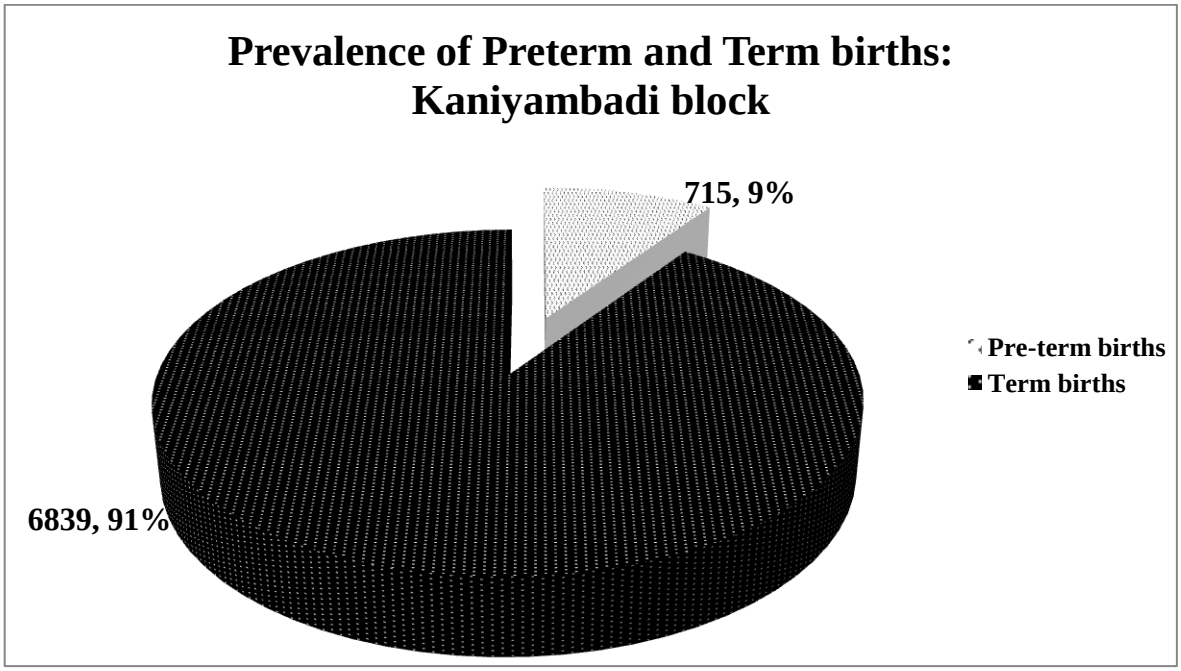


Figure 6.3 Prevalence of Preterm and Term births between the years 2001 to 2005 in Kaniyambadi block (N = 7554)

The inclusion criteria were:

- Children born between the years 2001 to 2005 who were born at less than 37 weeks of gestation (exposed group) and more than 37 weeks of gestation (unexposed group)
- Currently alive and are permanent residents of Kaniyambadi block

- Have a parent or a primary care-giver (other than father or mother), who is willing to consent to participate in the study.

The exclusion criteria were (for both the exposed and the unexposed group):

- Birth asphyxia
- Congenital heart disease
- Complex seizure disorders
- Documented inborn errors of metabolism
- Endocrine disorders
- Profound Mental retardation
- Severe physical disabilities

A total of 512 children were approached to participate in the study. These children were chosen by choosing a random sample using a random numbers table. The location of each child eligible to participate in the study was identified and the home visited with the help of the corresponding Area HA or the PTCHW.

Out of the children 406 children recruited into the study, 202 were preterm born children (exposed arm) and 204 were term born children (unexposed arm). Children were not recruited in the study because of reasons such as having moved out of area recently, out of station or neither the parent nor the primary care-giver was available at that point of time.

The children recruited from Kaniyambadi block were recruited from 45 villages. The following areas were the villages from where recruitment of study participants was done:

Kamrajnagar	Kaniyambadi	Sathumathurai	Edayansathu	Pangalathan
Kattuputhur	Tuthipet	Kurumburpalayam	Ramalinganagar	Sanjivipuram
Veppampet	Kattupadi	Sathupalayam	Bagayam	Rickshawcolony
Dharmavaram	Pennathur	Kilarasampet	Mettupalayam	Ganesapuram
Ganesapuram	Kesavapuram	Nelvoy	Sanjeevipuram	Perumalaipet
Allivaram	Sowdalipuram	Virupakshipuram	Nayanakannunagar	Sirukalambur
Nanjukondapuram	Adukamparai	Palavansathukuppam	Sirukalambur	Pangalathan
Puthur	Mettuadukamparai	Gandhinagar	Kilpallipet	Nambirajapuram
Papanthopu	Dahramavaram	Kannadipalayam	Edigaithopu	Kaligapuram

The eligible participants along with their parents or the primary caregiver were approached and invited to participate in the study. During this meeting, the details of the study were explained to them in detail in their own language and their willingness to participate in the study was confirmed. The parent's or the caregiver's consent and the child's assent was then obtained. If the eligible household was found to be locked or the parent or the primary caregiver was not available, the next eligible household was approached.

An interview was conducted with the parent or the primary caregiver. Basic socio-demographic data was collected. Antenatal, natal and postnatal details were obtained from both by the antenatal folder available with them and/or by recall in cases. Anthropometric measurement including weight (kg), height (cm) and mid-arm circumference for the child were obtained using standardized weighing scale and measuring tape. The screening tool (Brief Intellectual Disability Scale – BIDS) was administered by a single interviewer who was trained by the Department of Child and Adolescent Psychiatry to administer the questionnaire.

BIDS (Brief Intellectual Disability Scale) score >5 is said to be screen positive for intellectual disability with a sensitivity of 71.53% and a specificity of 80.95%. BIDS (Brief Intellectual Disability Scale) score > 11 is said to be diagnostic for intellectual disability with a sensitivity of 54.29% and a specificity of 100.00%.

The BIDS questionnaire had a total of ten questions. The responses to the BIDS questionnaire was recorded in the form of Likert scale as “Not true”, “Sometimes true” or “Very true” for the all the children born by preterm and term birth by the parent or the primary caregiver (Table 6.1). These responses were recorded for the 10 questions of the BIDS questionnaire (Annexure I).

Table 6.1 Scoring for the 3 responses to the questions of the BIDS questionnaire

Response to the BIDS questionnaire	Score
Not true	0
Sometimes true	1
Very true	2

Those who were screened using the validated screening questionnaire for intellectual disability (Brief Intellectual Disability Scale) and were found to have a BIDS score of more than 5 (probable intellectual disability) were offered referral to the Department of Child and Adolescent psychiatry for further evaluation. Those who were found to have a a BIDS score greater than 11 were offered referred to the Department of Child and Adolescent psychiatry for further management. The importance of the referral was explained to the parents especially on how the further evaluation and management might benefit their child in future.

6.10 Data entry and analysis

Data was entered using EpiData Entry (Data Management and basic Statistical Analysis System, Odense Denmark, EpiData Association, 2000-2008) and analysed using SPSS version 20.0 software, licensed for use by the Department of Community Health, Christian Medical College, and Vellore.

The WHO Anthro plus software was used to compute BMI (Body Mass Index) and thereby the Body Mass Index for age Z-score was further computed, from the recorded height and weight for the children.

6.11 Variables

Baseline socio-demographic correlates, antenatal details, birth history details, Anthropometry and Brief Intellectual Disability Scale (BIDS) were categorised accordingly either as a standard categorisation or using the inter-quartile ranges. This was done to ensure comparability.

- All the children belonged to the age group of 8 to 13 years. They were further categorized as:
    a) Less than 11 years
    b) More than 10 years
    a) The Socio-economic class of the study participants were calculated and classified using the Kuppusamy's scale, modified in 2013 (Annexure II).
    b) Upper
    c) Upper middle
    d) Lower middle
    e) Upper lower
    f) Lower

- Income was classified with the median monthly income of the study population as
    a) < Rs 5000 per month
    b) >= Rs 5000 per month
- Age of the mother at the birth of the child was classified with the median age as:
    a) < = 23 years
    b) > 24 years

- Age of the father at the birth of the child was classified with the median age as:
    a) < =31 years
    b) > 32 years
- Packed cell volume at the time of pregnancy for the mother was classified based on the WHO definition of Anaemia which was a PCV of less than 33% as:
    a) < 33% - Anaemia
    b) >= 33% - No Anaemia

    Anaemia was further classified (WHO classification) as:

    a) Mild – 30.0% - 33.0%
    b) Moderate – 21.0% - 30.0%
    c) Severe – Less than 21%
    d) Very severe – Less than12.0 %
- Preterm born children were further classified based on their gestation as follows:
    a) Extremely preterm (<28 weeks)
    b) Severe preterm (28-31 weeks)
    c) Moderate preterm (32-33 weeks)
    d) Late preterm (34-36 weeks) (21)

- Birth weight of the preterm and term children was classifies based on the WHO cut-offs as follows:
    a) Low birth weight (< 2.5 kg)
    b) Normal birth weight (>= 2.5 kg)

  The low birth weight of both the preterm and term born children were further classified as:
    a) Low birth weight (1500 to 2500 gram)
    b) Very low birth weight (1000 to 1500 gram)
    c) Extremely low birth weight (Less than 1000 gram)

- Body Mass Index (BMI) was calculated for all the children. The children with a Body mass index for age Z-score that were between 1SD TO -2SD were taken as normal for their age.

  The WHO Body mass index for age Z-score was used to classify thinness in the preterm and term born children:
    a) BMI-for-age Z-score < -2SD = Thinness
    b) BMI-for-age Z-score < -3SD = Severe Thinness

  The WHO Body mass index for age Z-score was used to classify thinness in the preterm and term born children:
    a) BMI-for-age Z-score > 1SD = Overweight
    b) BMI-for-age Z-score > 2SD = Obese
- BIDS score of 5 was the cut-off for screen positivity for Intellectual disability:
    a) Screen positive (>= 5)
    b) Screen negative(< 5)

- BIDS score of 11 was taken as the diagnostic cut-off for intellectual disability:
    a) Intellectually disabled (>=11)
    b) Not intellectually disabled (<11)

Figure 6.4 Flowchart showing various stages in the selection of the study participants

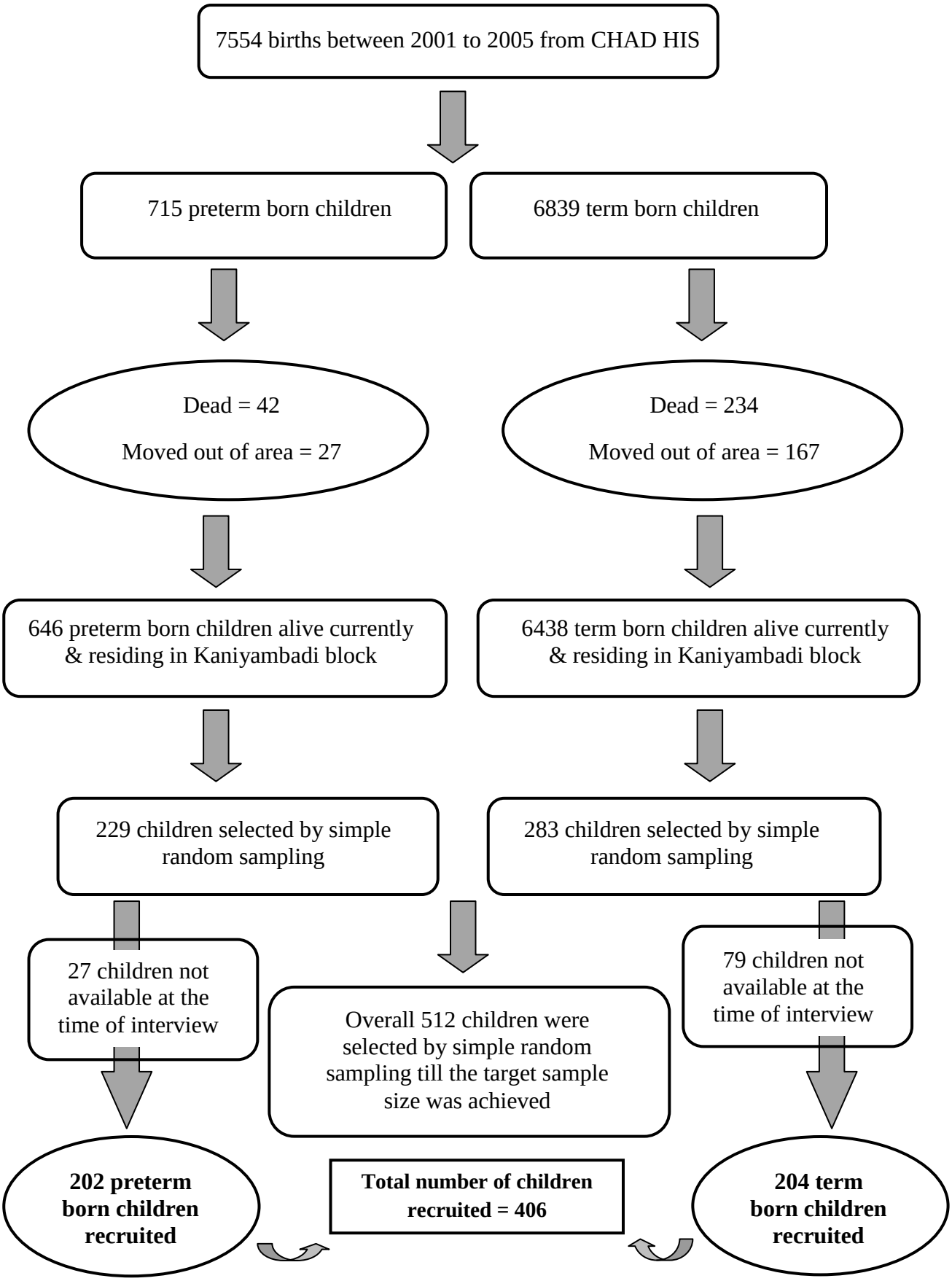
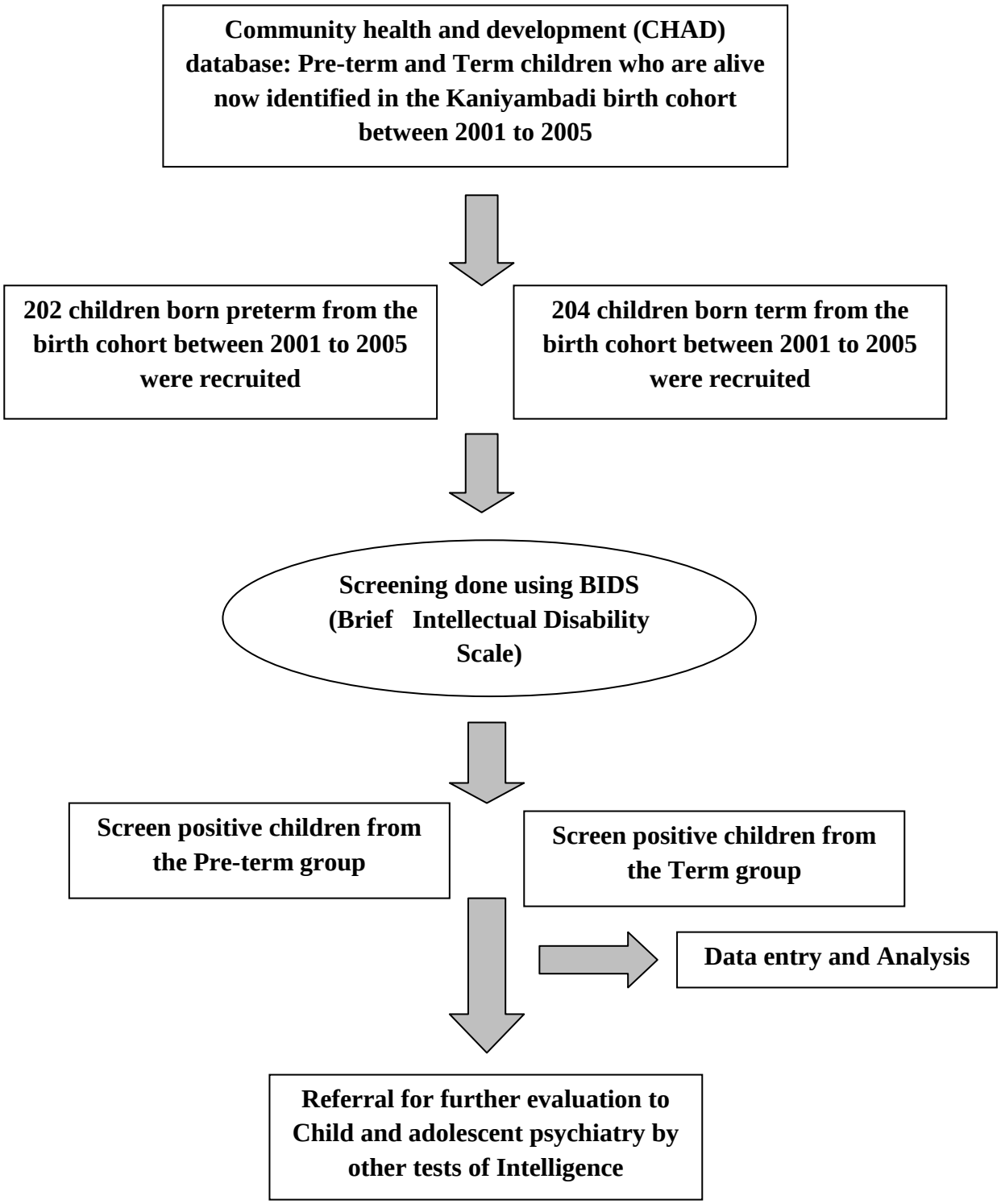


Figure 6.5 Flowchart of the study plan



7. Results

512 children comprising of 229 preterm born and 283 term born children were approached to participate in the study. Out of these children, 406 children were recruited to participate in the study. The remaining 106 children (27 preterm born and 70 term born) were not recruited for the study because of reasons such as having moved out of area recently, out of station, child not being available at home during the home visit or neither the parent nor the primary care-giver was available at that point of time.

Out of the 406 children recruited, 202 were preterm born children (exposed arm) and 204 were term born children (unexposed arm) who satisfied the major inclusion criteria.

7.1 Age of the participants

All the children in the study belonged to the age group of 8 to 13 years. The child's age was calculated as the number of completed years. The age group that had the least number of children were those in the 8 year age group. This was noted for both the preterm born as well as the term born children (Table 7.1). There was no statistically significant difference in the mean ages of the preterm and term born children (T-test value = 0.98, $p > 0.05$)

Table 7.1 Age distribution among the study participants

Age of the child (years)	Preterm born children (n=202)		Term born children (n=204)	
	Frequency	Percentage	Frequency	Percentage
8	9	4.5	9	4.4
9	48	23.8	38	18.6
10	45	22.3	42	20.6
11	32	15.8	39	19.1
12	40	19.8	40	19.6
13	28	13.9	36	17.6
Total	**202**	**100**	**204**	**100**

Chi square value = 2.947, p > 0.05

7.2 Gender of the participants

Among the preterm born children 110 (54.5%) were males. Among the term born children, 107 (52.5%) were females. There were more male children in the preterm born group and more female children in the term born children group. This difference was not however statistically significant. (Table 7.2)

Table 7.2 Gender distribution among the study participants

Sex	Preterm born children (n=202)		Term born children (n=204)	
	Frequency	Percentage	Frequency	Percentage
Male	110	54.5	97	47.5
Female	92	45.5	107	52.5

Chi square = 1.937, p > 0.05

7.3 Primary caregiver

Among the 406 children, 18 children did not have one of the parents alive at present. Among these, 15 children did not have their father alive currently (9 children born by preterm birth and 6 children born by term birth) and 3 children did not have their mother alive at present (2 children born by preterm birth and 1 child born by term birth).

28 children were taken care of by caregivers other than mother or father (20 children born by preterm birth and 8 children born by term birth). The caregivers were predominantly grandparents, aunts or elder siblings. Parents were not the primary caregiver in situations such as the mother not being alive or one or both the parents being away from the child because they were working out of station.

Aunts (50%) were the pre-dominant caregivers for the preterm born children, the others being grandmothers or elder sisters or elder brothers and occasionally a step-mother. Grandmothers (62.5%) were the common caregivers for children born by term birth, the others being uncles or elder sisters or elder brothers (Table 7.3).

Table 7.3 Type of primary care-givers other than parents among the preterm and term born children

Care-giver	Preterm born children (n=20)		Term born children (n=8)	
	Frequency	Percentage	Frequency	Percentage
Grandmother	4	20	5	62.5
Aunt	10	50	0	0
Uncle	0	0	1	12.5
Elder sister	4	20	1	12.5
Elder brother	1	5	1	12.5
Step-mother	1	5	0	0
Total	**20**	**100**	**8**	**100**

7.4 Education

The education of the either the parent (either of the parents who had the highest education) or the primary care-giver (in situations where the parents were not the primary care givers) was considered. 100 (49.5%) of the parent/primary caregiver of the preterm born children and 111(54.4%) of the parent/primary caregiver of the term born children respectively had studied up to middle school. 40 parents (19.8%) in the preterm born and 21 parents in the term born age-groups (10.3%) did not receive formal education. There were 14 (6.9%) of the parents/caregivers who were graduates among the term born children whereas this was only 3 (1.5%) among the preterm born children (Figure 7.1). There was a significant difference in the various cadres of education of the parent / primary care-giver of the preterm and term born children (Table 7.4). There were a significantly higher proportion of parents with no formal education among parents of preterm born children (Table 7.5)

Table 7.4 Education profile of the parent / primary caregiver of the study participants

Education	Parent/Caregiver of preterm born children (n=202)		Parent/Caregiver of term born children (n=204)	
	Frequency	Percentage	Frequency	Percentage
Nil education	40	19.8	21	10.3
Primary School	13	6.4	14	6.9
Middle School	100	49.5	111	54.4
High School	31	15.3	31	15.2
Intermediate/post high school diploma	14	6.9	13	6.4
Graduate/Post graduate	3	1.5	14	6.9
Professional course/honours	1	0.5	0	0

Chi square = 14.674, p = 0.023

Figure 7.1 Education of the parent / primary care-giver

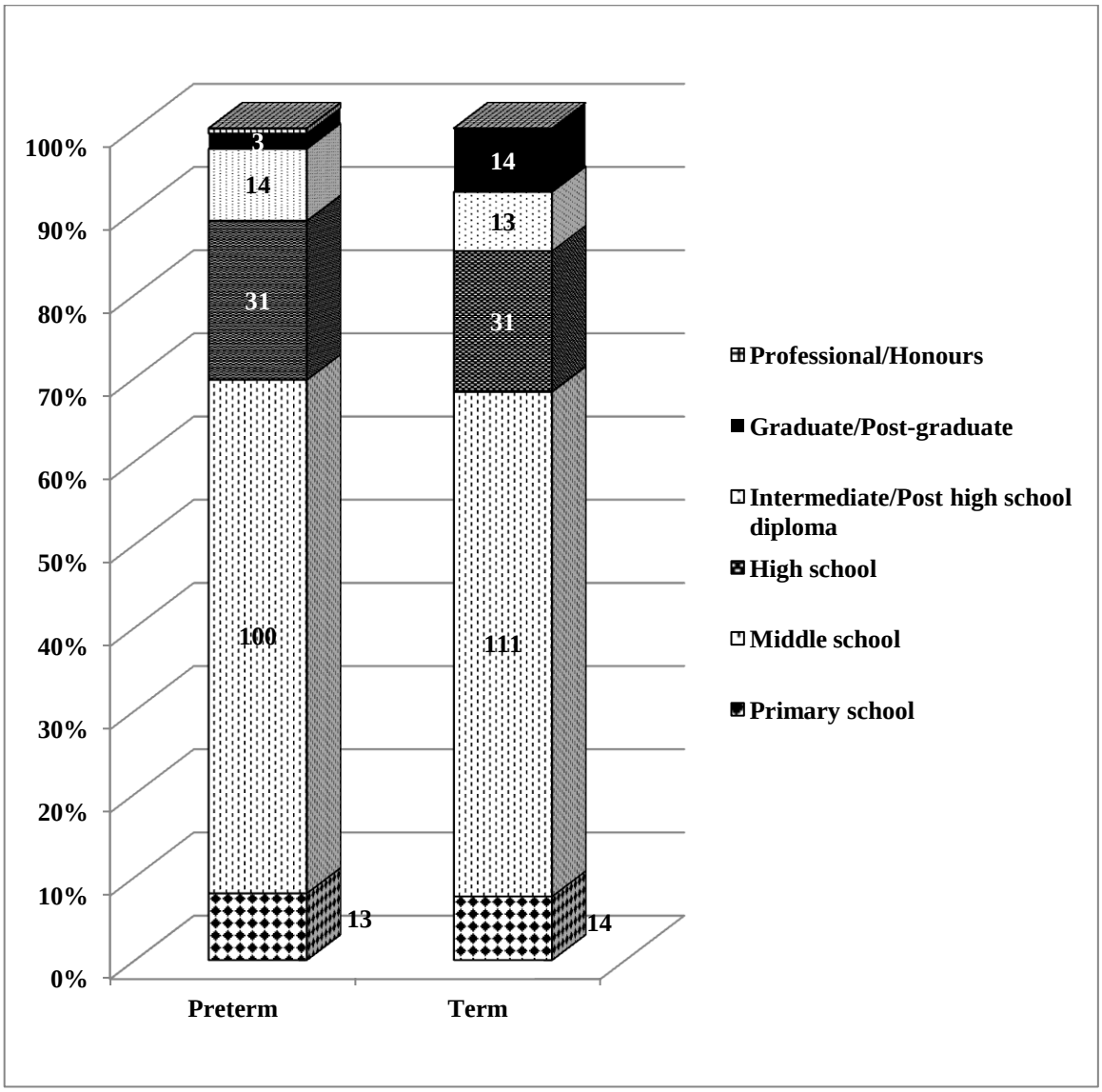


Table 7.5 Relationship between education of the parent / primary caregiver and preterm birth

Education	Preterm born children (n=202)		Term born children (n=204)	
	Frequency	Percentage	Frequency	Percentage
Not educated	40	19.8	21	10.3
Educated	162	80.2	183	89.7

Chi square = 7.187, p = 0.007

7.5 Occupation

Most of the family heads were semi-skilled workers, both among the preterm and the term born group. This included 67 (33.2%) and 81 (39.7%) in the preterm and term groups respectively. The next largest group were unskilled workers among both the preterm and term group56 (27.7%) and 64 (31.4%) respectively. The others were clerical/Shop owner/Farmers, 55 (27.2%) and 26 (12.7%) in the preterm and term born groups respectively. There were very few semi-professionals in both the preterm and term groups. 2 (1.0%) and 4 (2.0%) were unemployed in the preterm and term groups respectively. There was a significant difference in the different occupations of the head of the families between the preterm and term born children (Table 7.6).

Table 7.6 Occupational profile of the head of the family of the preterm and term born children

Occupation	Parent/Caregiver of preterm born children (n=202)		Parent/Caregiver of term born children (n=204)	
	Frequency	Percentage	Frequency	Percentage
Unemployed	2	1.0	4	2.0
Unskilled	56	27.7	64	31.4
Semi-skilled	67	33.2	81	39.7
Skilled	12	5.9	6	2.9
Clerical/Shop owner/Farmer	55	27.2	26	12.7
Semi-profession	9	4.5	19	9.3
Profession	1	0.5	4	2.0
Total	**202**	**100**	**204**	**100**

Chi square = 20.269, p = 0.002

7.6 Monthly family income

The monthly income of the families of preterm and term born children was obtained. These incomes were classified as per the Kuppusamy's scale that was modified in the year 2013. This was also done by taking the Consumer price index (CPI) into consideration to account for the increase in the prices of various commodities as a consequence of increased consumption as well as inflation since the original Kuppusamy's scale was formulated in the year 1976.

The mean (SD) family income of the preterm birth group was Rs 6149 (6280.6) per month and the incomes ranged from Rs 1000 per month to Rs 60000 per month. Similarly the mean (SD) family income among the term born children was Rs 6997.5 (4591.5) and it ranged from Rs 1000 to Rs 30000. There was no significant difference in the incomes of the preterm and term birth groups (T-test value = 0.368, p value > 0.05). However, 63.8% (129) of the preterm born children belonged to families who had a monthly income of less than Rs 5223 while only 50% (102) of the families belonging to term born children had similar incomes.

When the median of income was taken into consideration, 130 (55.8%) of the families belonging to the preterm born children had an income of less than Rs 5000 when compared to 103 (44.2%) of those belonging to the term born children. There was a significant association between the monthly family income of Rs less than 5000 with preterm birth (Chi square value = 7.980, $p < 0.05$) (Table 7.7)

Table 7.7 Relationship between monthly family income and preterm birth

Monthly income/Preterm or term	Preterm born children (n=202)		Term born children (n=204)	
	Frequency	Percentage	Frequency	Percentage
Rs < 5000	130	64.4	103	50.5
Rs > 5000	72	35.6	101	49.5

Chi square value = 7.980, p = 0.005

The risk of a preterm child being born in a family with a monthly family income of less than Rs 5000 was 1.7 times when compared those with a monthly family income of more than Rs 5000.

7.7 Socio-economic status of the participants

The socio-economic class of the study participants (Table 7.8) was derived from the socio-economic scores calculated as a summation of the highest education in the family, highest occupation in the family and the monthly income.

Socio-economic class of participants was classified using the Kuppusamy's scale. Among the preterm born children, the maximum number of participants (78.2%) belonged to the upper lower class and the same applied to the term born children (76.2%). There was no significant difference in the socio-economic class in both groups (Chi square value = 0.346, $p > 0.05$) (Table 7.9)

Table 7.8 Socio-economic class of participants, classified using Kuppusamy's scale

Socio-economic class	Parent/Caregiver of preterm born children (n=202)		Parent/Caregiver of term born children (n=204)	
	Frequency	Percentage	Frequency	Percentage
Upper	1	0.5	2	1.0
Upper-middle	9	4.5	10	4.9
Lower-middle	32	15.8	36	17.6
Upper-lower	158	78.2	156	76.5
Lower	2	1.0	0	0.0

Chi square value = 2.624, p > 0.05

Table 7.9 Relationship between Socio-economic class and preterm birth

Socioeconomic class/Preterm or term	Preterm born children (n=202)		Term born children (n=204)	
	Frequency	Percentage	Frequency	Percentage
Lower and upper lower	120	59.4	127	62.3
Lower middle and upper middle	182	30.6	77	37.7

Chi square value = 0.346, p >0.05

7.8 Characteristics of the study participants

7.8.1 Age of the parents at marriage and birth of the study participant

The median was taken as the cut-off point for classifying the ages of mothers and the fathers for the age at marriage and the age at the time of the birth of the study participant. The median cut-off for father and mother was 19 and 26 respectively.

116 (57.4%) of the preterm born children and 114 (55.9%) of the term born children had mothers who were married at less than 19 years of age. 114 (56.4%) of the preterm born children and 107 (52.5%) of the term born children had fathers who were married at less than 26 years of age. There was no significant association with either the age of the mother or the age of the father at marriage with preterm birth (Table 7.22).

111 (55.5%) of the preterm born children and 109 (53.7%) of the term born children were born to their mothers when they were less than 23 years of age. 110 (57.0%) of the preterm born children and 110 (55.6%) of the term born children were born when their fathers were less than 31 years of age. There was no significant association with either the age of the mother or the age of the father with preterm birth (Table 7.22).

7.8.2 Consanguinity of the parents

149 (37%) of the parents of all the participants were married consanguinously (Figure 7.2). This included 82 (40.6%) among the preterm born children and 67 (32.8%) among the term born children. There were more consanguineously married parents among the preterm born children than the term born children. This however was not statistically significant. (Table 7.22). Among the children born to consanguineously married parents, 110 (74.4%) were parents married by second degree whereas 39 (73.1%) were parents married by third degree consanguinity (Figure 7.3). Here second degree marriage was defined as marriage mainly between uncle and niece whereas third degree marriage was defined as marriage between cousins and other distant relatives. There was no significant association between the degree of consanguinity and preterm birth (Table 7. 22).

Figure 7.2 Marriage consanguinity of the parents

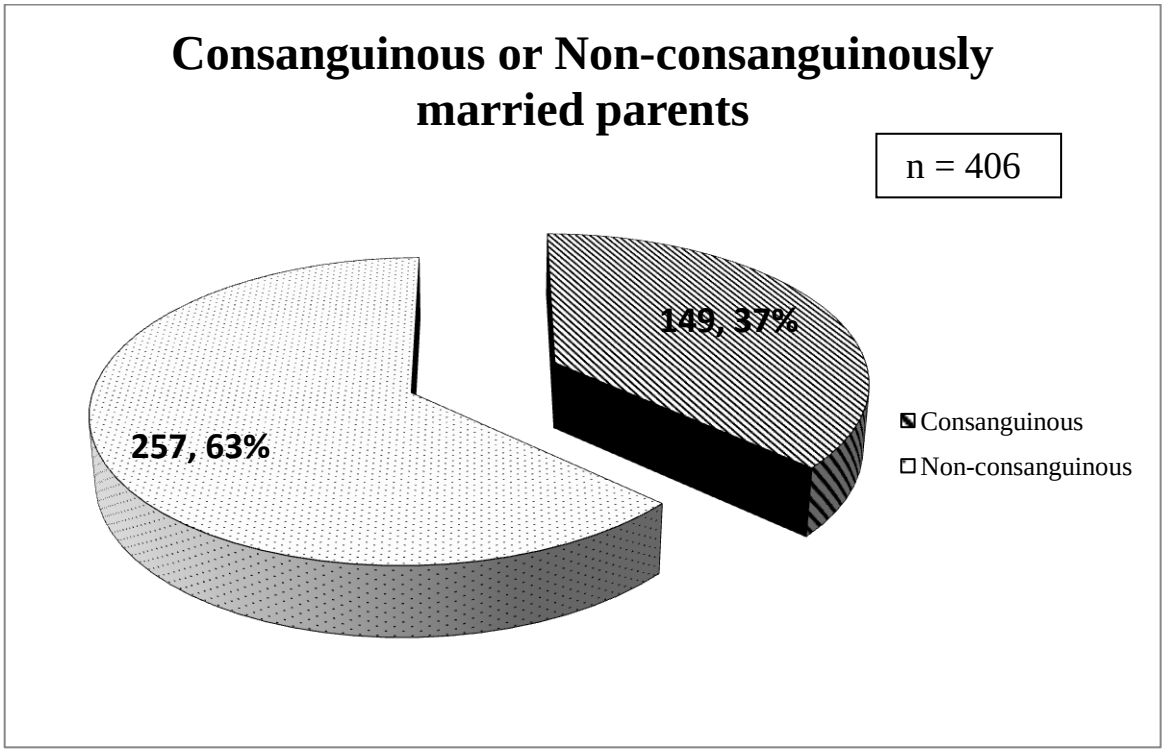
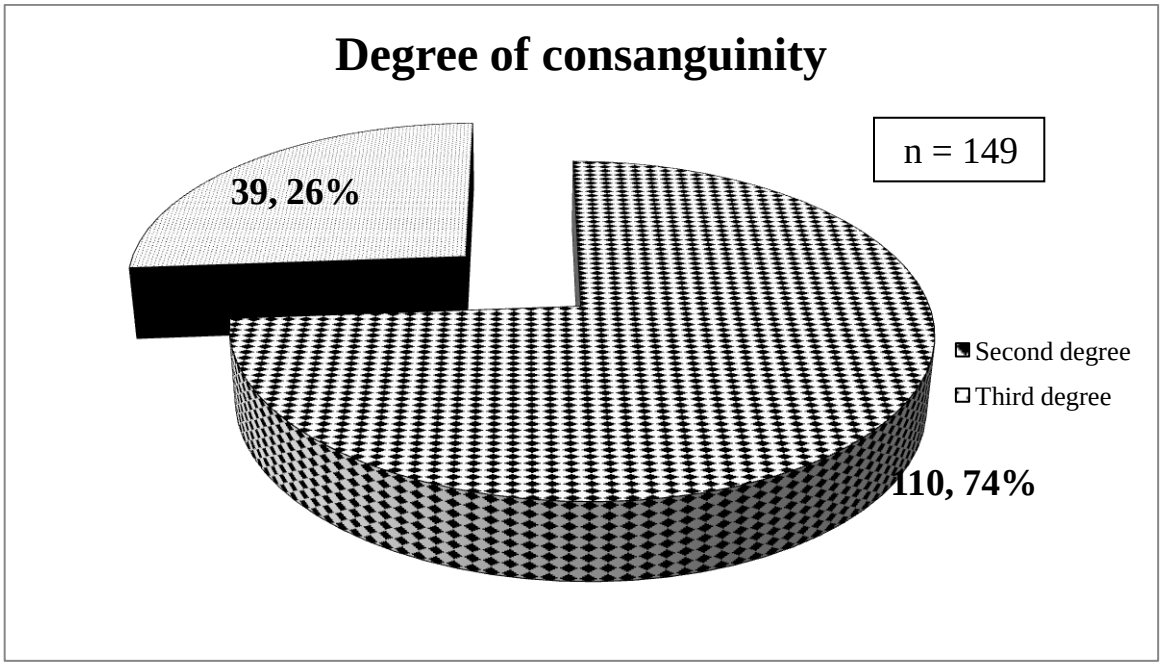


Figure 7.3 Degree of consanguinity of the parents



7.8.3 Primary infertility in the parents

11 (5.4%) of the preterm born children and 16 (7.8%) of the term born had parents who had a history of primary infertility (for more than 5 years). There were more children born term, whose parents had a history of primary infertility. There was no significant difference between preterm birth and a history of primary infertility among the parents (Table 7.22).

7.8.4 Underlying medical condition in the mother

11 (5.4%) of the mothers of preterm born children and 3 (1.5%) of the mothers of term born had an associated medical condition present prior to the birth of the child. This difference was statistically significant (Chi square value = 4.817, $p < 0.05$) (Table 7.22). The predominant medical condition among the mothers who delivered preterm children was Diabetes mellitus, the next being hypertension and the others included hypothyroidism, stroke, congenital heart disease and an underlying mental disorder. Among the mothers with term born children, the predominant medical condition was Diabetes mellitus (Table 7.10). There were more diabetic and hypertensive mothers among the preterm born children than the term born.

Table 7.10 Medical condition in the mother

Medical risk factor for mother	Preterm (n = 11)		Term (n = 3)	
	Frequency	Percentage	Frequency	Percentage
Diabetes Mellitus	4	66.7	2	33.3
Hypertension	3	100	0	0
Hypothyroidism	1	50	1	50
Cardiac disease	1	100	0	0

Stroke	1	100	0	0
Mental illness	1	100	0	0

7.8.5 Antenatal risk factor

Among the preterm born children, 15 (7.4%) of their mothers had an underlying antenatal risk factor for that pregnancy when compared to the term born children who had 8 (3.9%) of their mothers having the same. There was no significant association between the presence of an antenatal risk factor in the mother and the birth of a preterm child (Table 7.22). The predominant antenatal risk factors in the mothers with preterm born children were Pre-eclampsia / eclampsia and twin pregnancy (Table 7.11).

Table 7.11 Type of antenatal risk factor for the mother

Antenatal risk factor for mother	Preterm (n = 18)		Term (n = 8)	
	Frequency	Percentage	Frequency	Percentage
Pre-eclampsia/Eclampsia	6	66.7	3	33.3
Pregnancy Induces Hypertension (PIH)	1	100	0	0
Gestational Diabetes Mellitus (GDM)	2	40	3	60
Twin pregnancy	6	75	2	25

7.8.6 Antenatal visits

WHO recommends at least four antenatal visits that include Tetanus toxoid immunization at the earliest, detection and the appropriate management of common infections in pregnancy and the early detection of danger signs in the pregnant woman.

In our study, 461 mothers (88.9%) had more than four antenatal visits during their pregnancy for the study participant. 32 (15.8%) of the mothers of preterm born children

had less than 4 antenatal visits in comparison to 13 (6.4%) mothers with term born children who had more than 4 antenatal visits. Mothers of preterm born children had fewer antenatal visits when compared to their term counterparts. There was a significant association between fewer antenatal visits and preterm birth (Table 7.22).

However this may be a spurious association because mothers who have had preterm deliveries would tend to have had fewer antenatal visits when compared to their term counterparts as a direct consequence of labour. The antenatal visits in early pregnancy are fewer (once in 4 – 6 weeks) when compared to frequent antenatal visits in late pregnancy (Once in 1 – 2 weeks).

7.8.7 Family history of Intellectual disability

8 (4.0%) of the preterm born children had a family history of intellectual disability when compared to 11 (5.4%) of the term born. There was no significant association between a family history of intellectual disability and preterm birth (Table 7.22).

Among the preterm and term born children, there were 4 and 5 cousins who had intellectual disability respectively. Also there were 2 and 5 aunts/uncles who had intellectual disability among the preterm and term born children respectively (Table 7.12).

Table 7.12 Member of the family with Intellectual disability

Member of the family with Intellectual disability	Preterm (n = 8)		Term (n = 11)	
	Frequency	Percentage	Frequency	Percentage
Cousin	4	50.0	5	45.4
Uncle / Aunt	2	25.0	5	45.4
Father	2	25.0	1	9.2

7.8.8 Intellectual disability among siblings

A total of 10 children had siblings with a history of intellectual disability. Among these children, 8 (4.0%) of the preterm born children and 2 (1.0%) of the term born children had a sibling with intellectual disability. This association narrowly missed statistical significance (Table 7.22).

4 preterm born children and 2 term born children had their elder brother with intellectual disability. The remaining among the preterm born with intellectual disability were 3 elder sisters and one younger sister (Table 7.13).

Table 7.13 Intellectual disability among siblings

Sibling with Intellectual disability	Preterm (n = 8)		Term (n = 2)	
	Frequency	Percentage	Frequency	Percentage
Elder brother	4	50.0	2	100
Elder sister	3	37.5	0	0
Younger sister	1	12.5	0	0

7.8.9 Anaemia

Mothers of the preterm and term born children, during their pregnancy were classified as anaemic or not anaemic using the WHO definition of anaemia in pregnancy.

The PCV value was obtained from the antenatal folder that was available with the mother during the home visit to recruit the participant. This was available only for 88 of the

preterm born mothers and 103 of the term born mothers. 40 (47.6%) of the mothers with preterm born children and 50 (48.5%) of the mothers with term born children were anaemic (PCV < 33.0%). There was no significant association between anaemia and preterm birth (Chi square value = 0.509, p >0.05) (Table 7.22).

24 (60.0%) of mothers with preterm born children and 42 (84.0) of the term born children had mild anaemia and 15 (37.5%) and 8 (16.0%) had moderate anaemia respectively. Only one mother with a preterm born child had severe anaemia.

7.9 Place of delivery

CHAD hospital was the commonest place of delivery among both preterm and term born children (59.4% of preterm born children and 59.85 of the term born children). This was because CHAD hospital historically has offered maternal and child health services to the population of Kaniyambadi block. The other places of delivery were CMC hospital, GVMCH, PHC and other private centres.

40 (19.8%) preterm born children delivered at home. Among term born children 30 (14.7%) delivered at home. This may be because majority of the preterm deliveries are spontaneous or precipitate (Table 7.14).

Table 7.14 Place of delivery among the preterm and term born children

Place of delivery	Preterm born children (n=202)		Term born children (n=204)	
	Frequency	Percentage	Frequency	Percentage
CHAD hospital	120	59.4	122	59.8
CMCH	15	7.4	13	6.4
PHC	12	5.9	14	6.9
GVMCH	7	3.5	6	2.9

Private hospital	6	3.0	7	3.4
Home delivery	40	19.8	30	14.7
Others	2	1.0	12	5.9

7.10 Mode of delivery

The most common mode of delivery for both the preterm and term born children was normal vaginal delivery. There were more breech extractions and LSCS among the preterm born (2.5% and 9.9% respectively) when compared with the term born (0.5% and 6.3% respectively) (Table 7.15).

Table 7.15 Mode of delivery among the preterm and term born children

Mode of delivery	Preterm born children (n=202)		Term born children (n=204)	
	Frequency	Percentage	Frequency	Percentage
Normal vaginal delivery	175	86.6	185	90.7
Suction cup extraction	1	0.5	4	2.0
Forceps extraction	1	0.5	1	0.5
Breech extraction	5	2.5	1	0.5
LSCS	20	9.9	13	6.3

7.11 Baby cried at birth

Among the 202 preterm children, 9 (4.5%) of the children did not cry. All term born children cried at birth. There was a significant association between preterm birth and the child not having cried at birth (Fisher's exact <0.05) (Table 7.16).

Table 7.16 Relationship between baby crying at birth and preterm birth

Baby cried at birth	Preterm born children (n=202)		Term born children (n=204)	
	Frequency	Percentage	Frequency	Percentage
No	9	4.5	0	0
Yes	193	0	204	100

Fisher's exact = 0.002

7.12 Seizures within 24 hours of life

Among preterm born children, 3 (1.5%) had seizures within the first 24 hours of birth in comparison to 1 (0.5%) child among the term born children. There was no significant association between preterm birth and the onset of seizures within the first 24 hours of birth (Fisher's exact > 0.05) (Table 7.17).

Table 7.17 Relationship between seizures (within first 24 hours of birth) and preterm birth

Seizures within 24 hours of birth	Preterm born children (n=202)		Term born children (n=204)	
	Frequency	Percentage	Frequency	Percentage
Yes	3	1.5	1	0.5
No	199	98.5	203	99.5

Fisher's exact > 0.05

7.13 Stratification of the preterm born children by their gestational age at birth

The preterm born children were stratified using the WHO classification of preterm births. Majority of the preterm born children 149 (73.8%) were late preterms. The remaining was

constituted by 26 (12.9%) moderate preterms and 24 (11.9%) severe preterms. There were 3 (1.5%) preterms who were born extremely preterm (Table 7.18).

Table 7.18 Stratification of the preterm born children by their gestational age

Gestation period	Frequency	Percentage
< 28 weeks (Extremely Preterm)	3	1.5
28 to 31 weeks (Severe Preterm)	24	11.9
32 to 33 weeks (Moderate Preterm)	26	12.9
34 to 36 weeks (Late Preterm)	149	73.8
Total	**202**	**100**

7.14 Low birth weight

Birth weights were obtained for both the preterm and term born children from the CHAD base hospital database. The birth weights were classified as low birth weight and normal birth weight in accord to the WHO definition and low birth weight was further classified using the WHO classification.

90 (44.6%) of the preterm children born were of low birth weight when compared to 25 (12.3%) of the term born children (Figure 7.6). There was a significant association between preterm birth and low birth weight (Chi square value =52.15, p <0.001) (Table 7.19).

Among the preterm born low birth weight children, 72 (80.0%) were of borderline low birth weight, 13 (14.4%) were of very low birth weight and 5 (5.6%) were of extremely low birth weight. Among the term born children 24 (96%) were of borderline low birth weight and 1 (4%) was of extremely low birth weight. There were no very low birth

weight children among the term born children (Figure 7.4, 7.20). There were more numbers of low birth weight, very low birth weight and extremely low birth weight among the preterm born children when compared to the term born children.

Table 7.19 Association between preterm birth and low birth weight

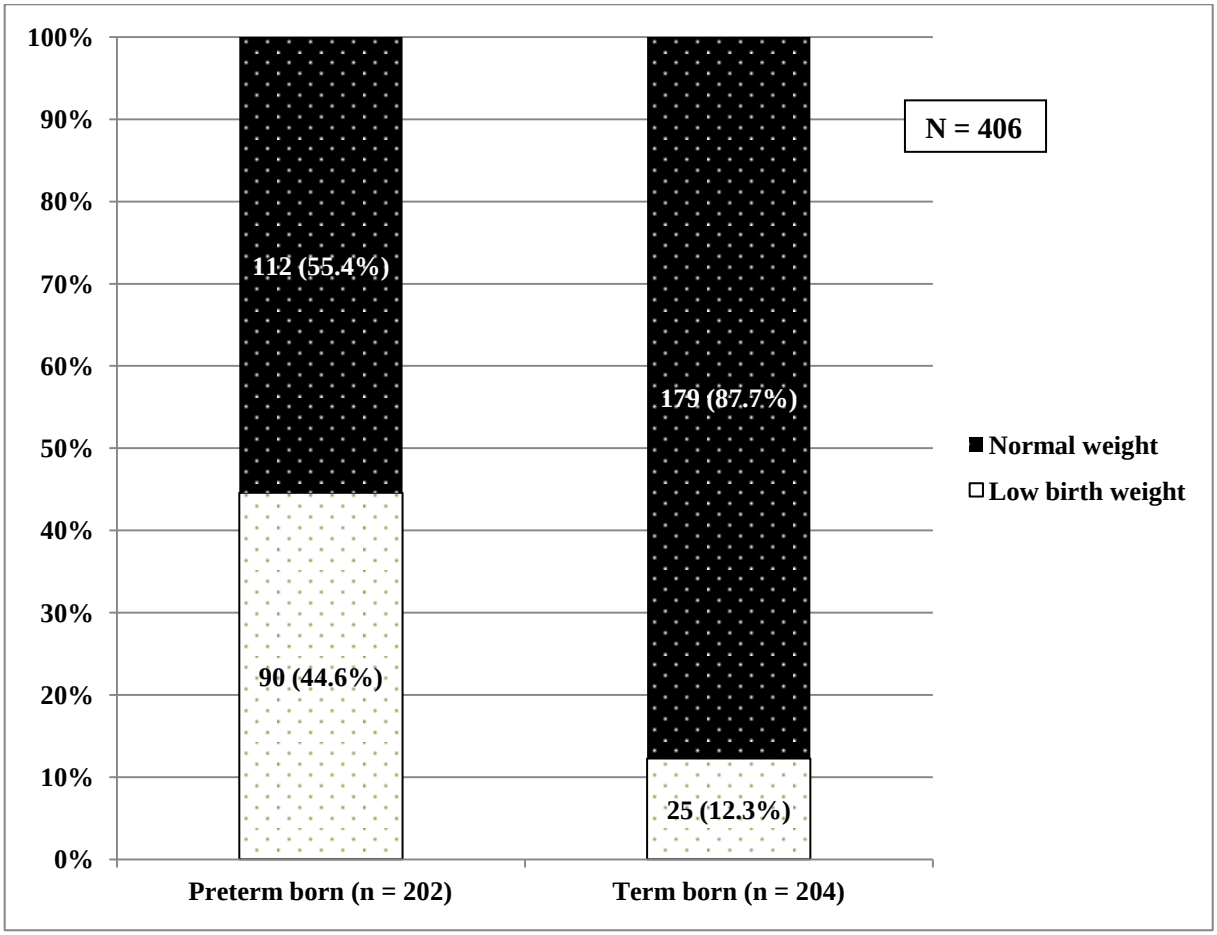
Normal / Low birth weight	Preterm born children (n=202)		Term born children (n=204)	
	Frequency	Percentage	Frequency	Percentage
Low birth weight	90	44.6	25	12.3
Normal birth weight	112	55.4	179	77.2

Chi square value =52.15, p = 0.000

Table 7.20 Distribution of low birth weight among the preterm and term born children

Low birth weight classification	Preterm born children (n=90)		Term born children (n=25)	
	Frequency	Percentage	Frequency	Percentage
Low birth weight (1.5 – 2.5kg)	72	80.0	24	96.0
Very low birth weight (1.0 – 1.5kg)	13	14.4	0	0
Extremely low birth weight (<1.0kg)	5	5.6	1	4.0
Total	**90**	**100**	**25**	**100**

Figure 7.4 Graph showing proportion of Low birth weight among the preterm and term born children



7.15 Body mass index (BMI) for age Z-score

Anthropometry was obtained for 201 children that included standing height, weight and mid arm circumference. Anthropometry could not be measured for 5 children in the study since they were unavailable following the interview with the parent/primary caregiver.

BMI was computed for 202 children and was used to compute the Z-scores for these 202 children using the WHO Anthro plus calculator. The WHO standards were used to classify thinness and obesity with respect to the corresponding standard deviation.

Thinness was defined as a BMI-for-age Z-score being less than -2 SD and severe thinness being a BMI-for-age Z-score being less than -3 SD. Obesity was defined as a BMI-for-age Z-score being more than 2 SD. Those with a BMI-for-age Z-score between 1SD to -2SD were considered as normal for the age.

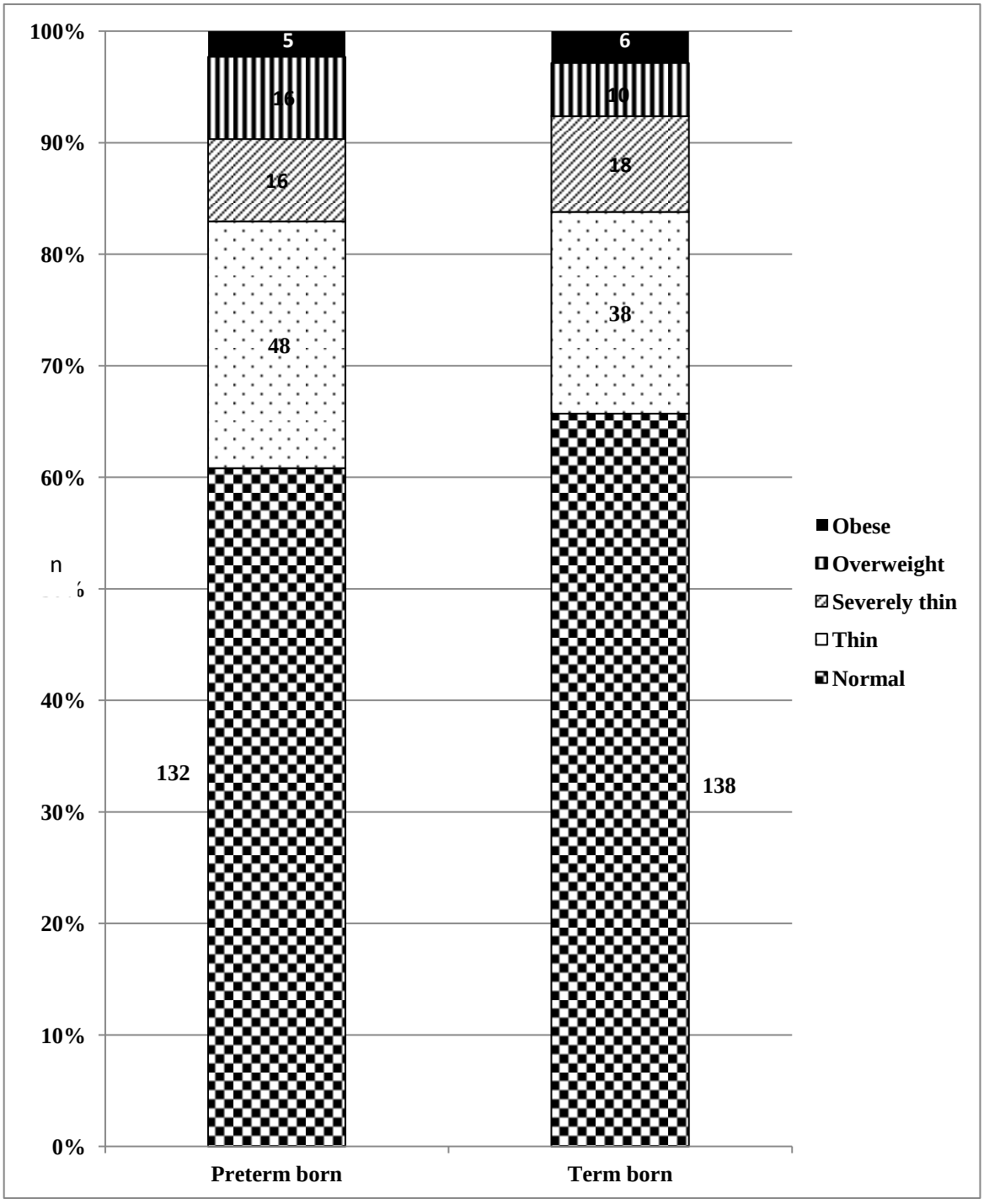
5 (2.5%) of the term children were obese in comparison to 6 (3.0%) of the term born children. Among the preterm born children 48 (23.8%) and 16 (8.0%) were thin and severely thin respectively when compared to 38 (19.0%) and 18 (9.0%) of their term counterparts respectively (Figure 7.5). There were no significant differences in the various BMI-for-age Z score between the preterm and term born children (Table 7.21).

Table 7.21 Prevalence of thinness and obesity among the preterm and term born children using BMI-for-age Z-score

Low birth weight classification	Preterm born children (n=201)		Term born children (n=200)	
	Frequency	Percentage	Frequency	Percentage
Normal	116	57.7	128	64.0
Thinness	48	23.9	38	19.0
Severe thinness	16	8.0	18	9.0
Overweight	16	8.0	10	5.0
Obese	5	2.5	6	3.0
Total	**201**	**100**	**200**	**100**

Chi square value =3.344, p > 0.05

Figure 7.5 Prevalence of thinness and obesity among the preterm (n = 64) and term (n = 56) born children using the BMI-for-age Z-score



Overall there was a significant association between presence of a medical condition in the mother, less than 4 antenatal visits and the presence of a sibling with a history of intellectual disability with preterm birth, thereby being important risk factors for same.

Table 7.22 Comparison of various characteristics among term and preterm births

Sl No.	Characteristics	Chi Square	p value
1.	Age of mother at marriage	0.098	0.754
2.	Age of the father at marriage	0.650	0.420
3.	Age of mother at birth of child	0.132	0.716
4.	Age of father at birth of child	0.082	0.774
5.	Consanguinity of the parents	2.625	0.105
6.	Second degree consanguinity	0.030	0.862
7.	Primary infertility	0.940	0.332
8.	Presence of a medical condition in the mother	-	**Fisher's = 0.032**
9.	Presence of an antenatal risk factor in the mother	2.332	0.127
10.	Antenatal visits less than 4	**9.234**	**0.002**
11.	Family history of intellectual disability	0.466	0.495
12.	Sibling with intellectual disability	-	**Fisher's = 0.061**
13.	Anaemia in the mother during pregnancy	0.016	0.900

7.16 Responses to the BIDS questionnaire

The responses to the BIDS questionnaire were recorded as described in the methodology (Tables 7.23 – 7.32, Figures 7.6 – 7.15).

Table 7.23 Responses to the BIDS question "Does he / she act too young for his age?"

BIDS question	Response	Preterm born		Term born	
		Freq	%	Freq	%
Act too young	Not true	183	90.6	203	99.5
	Sometimes true	7	3.5	0	0
	Very true	12	5.9	1	0.5

Chi square value =17.335, p = 0.000

Figure 7.6 Responses to the BIDS question "Does he / she act too young for his age?"

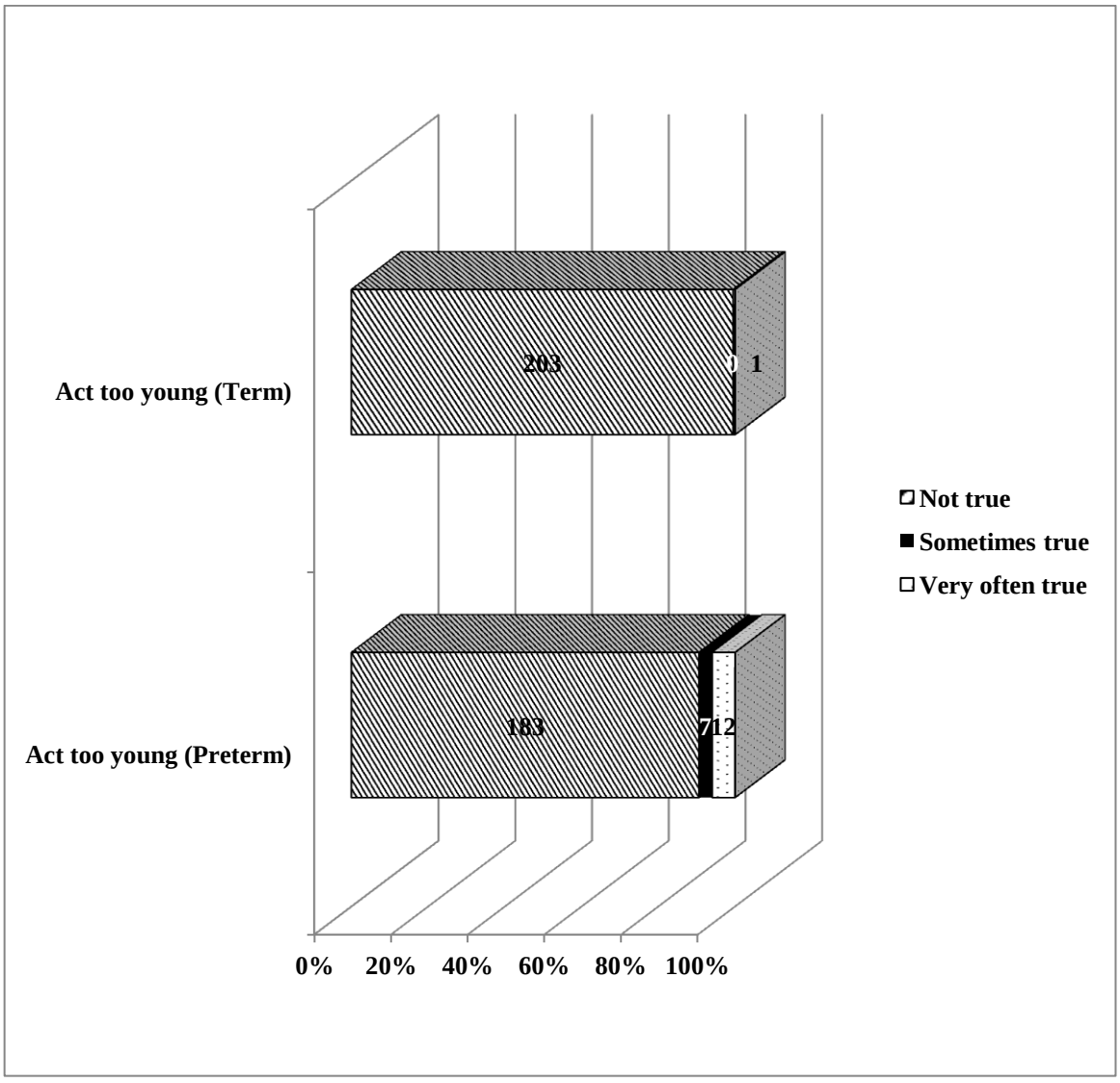


Table 7.24 Responses to the BIDS question "Does he / she suffer from poor school work?"

BIDS question	Response	Preterm born		Term born	
		Freq	%	Freq	%
Poor school performance	Not true	91	45.0	148	72.5
	Sometimes true	73	36.2	50	24.6
	Very true	38	18.8	6	2.9

Chi square value =41.159, p = 0.000

Figure 7.7 Responses to the BIDS question "Does he / she suffer from poor school work?"

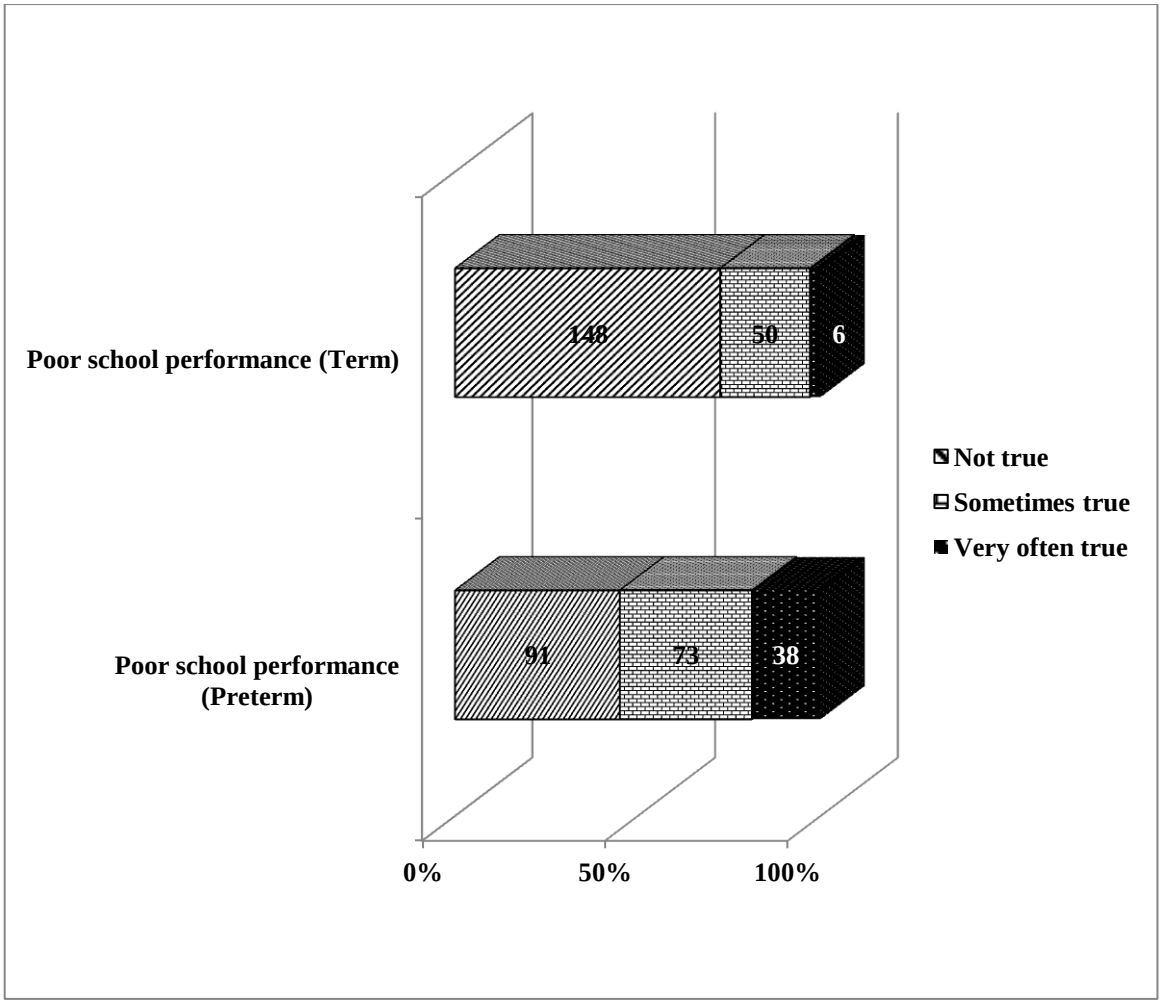


Table 7.25 Responses to the BIDS question "Does he / she find it difficult to concentrate?"

BIDS question	Response	Preterm born		Term born	
		Freq	%	Freq	%
Difficult to concentrate	Not true	143	70.8	185	90.7
	Sometimes true	7	3.5	6	2.9
	Very true	52	25.7	13	6.4

Chi square value =28.846, p = 0.000

Figure 7.8 Responses to the BIDS question "Does he / she find it difficult to concentrate?"

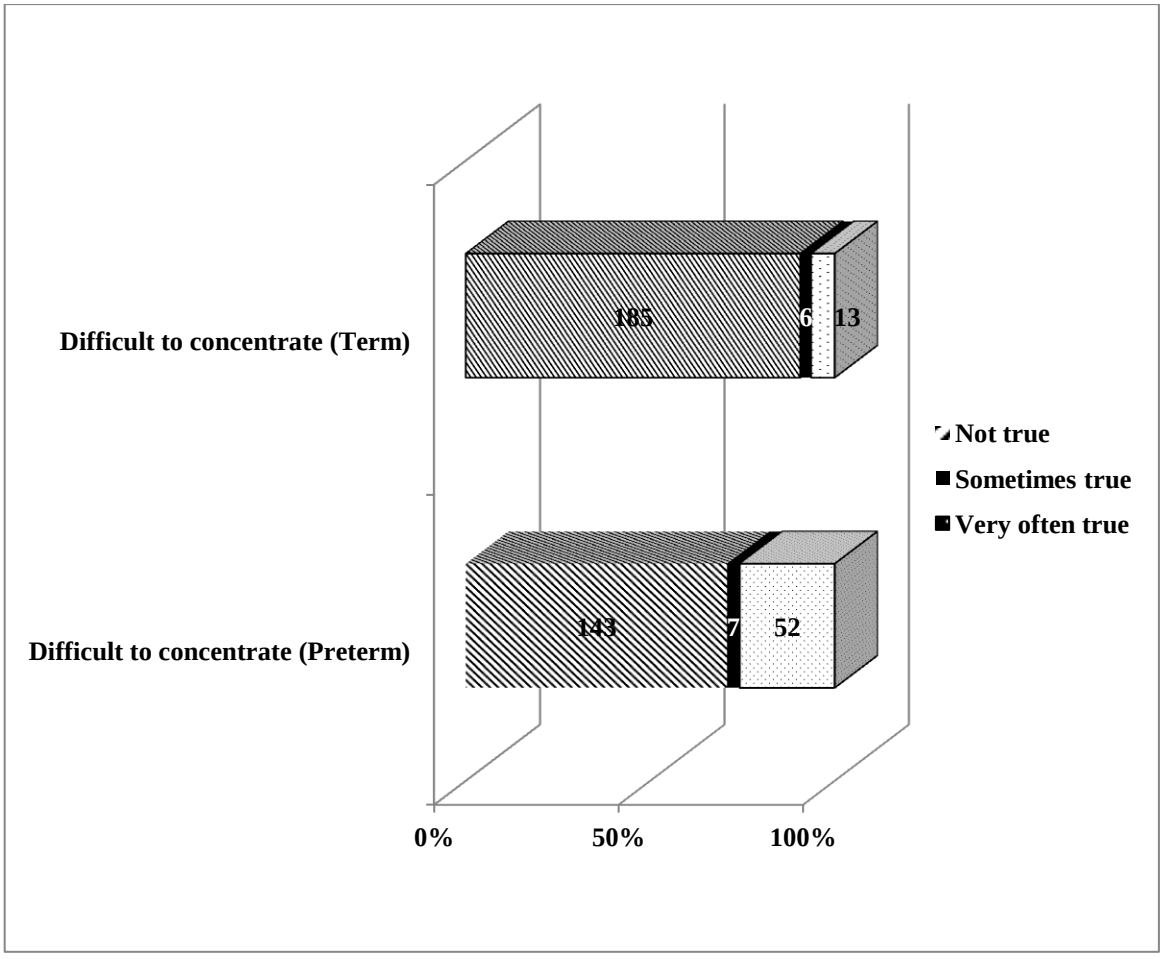


Table 7.26 Responses to the BIDS question "Does he / she get often teased by the others?"

BIDS question	Response	Preterm born		Term born	
		Freq	%	Freq	%
Often teased	Not true	167	82.7	201	98.5
	Sometimes true	5	2.5	0	0
	Very true	30	14.8	3	1.5

Chi square value = 30.223, p = 0.000

Figure 7.9 Responses to the BIDS question "Does he / she get often teased by the others?"

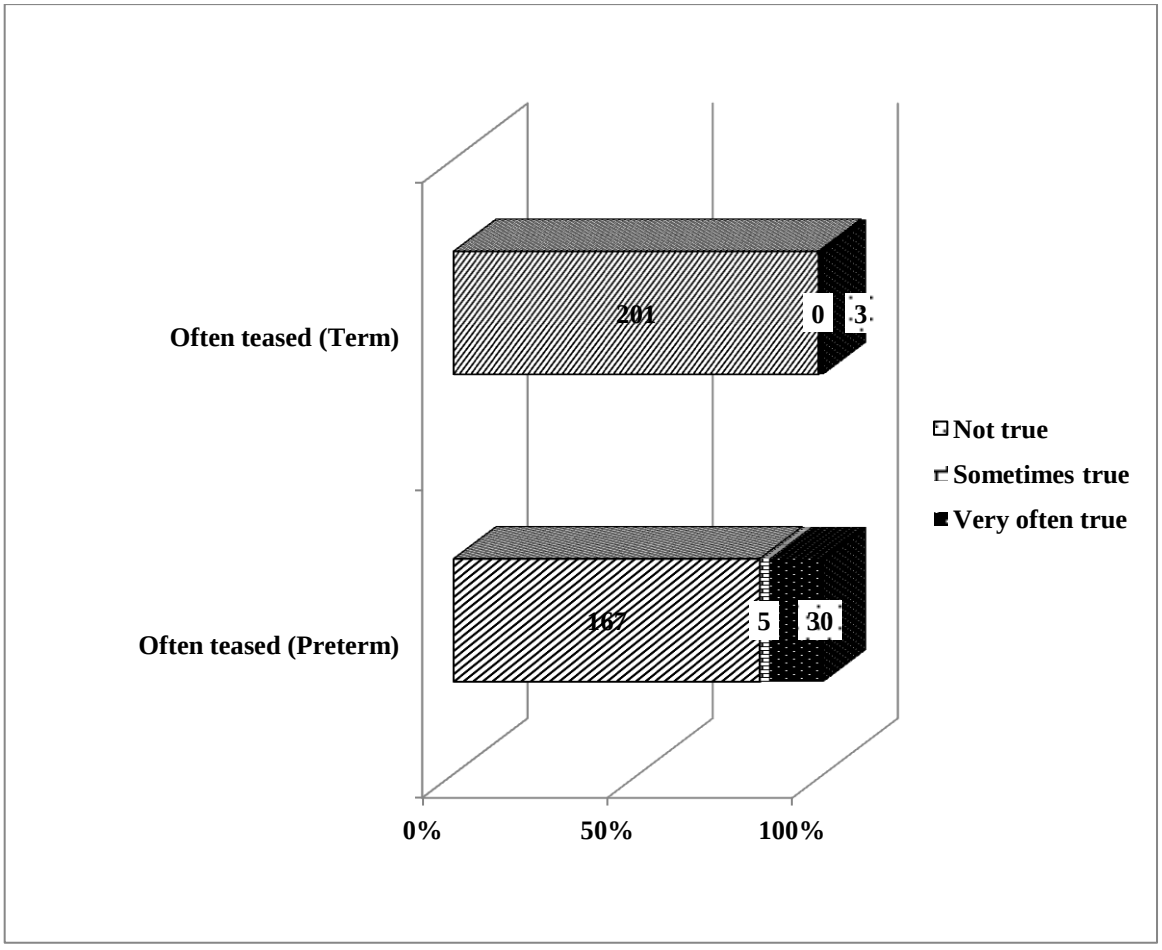


Table 7.27 Responses to the BIDS question "Does he / she suffer from speech problems?"

BIDS question	Response	Preterm born		Term born	
		Freq	%	Freq	%
Speech problems	Not true	180	89.1	194	95.1
	Sometimes true	7	3.5	6	2.9
	Very true	15	7.4	4	2.0

Chi square value = 6.960, p = 0.031

Figure 7.10 Responses to the BIDS question "Do he/she suffer from speech problems?"

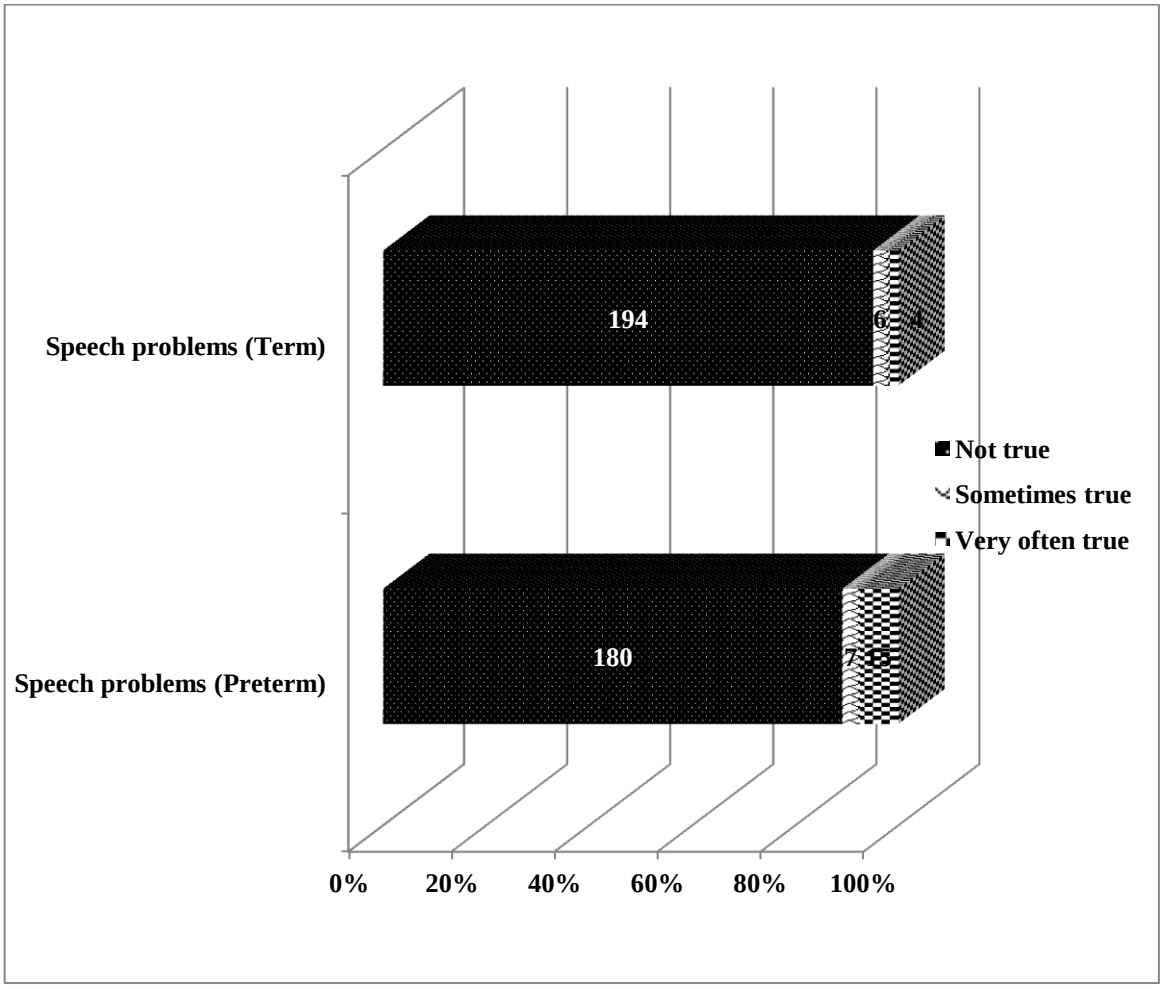


Table 7.28 Responses to the BIDS "Is he poorly coordinated or clumsy in various physical activities?"

BIDS question	Response	Preterm born		Term born	
		Freq	%	Freq	%
Clumsy	Not true	198	98.0	204	0
	Sometimes true	0	0	0	0
	Very true	4	0	0	0

Chi square value = 4.080, p < 0.043

Figure 7.11 Responses to the BIDS question "Is he poorly coordinated or clumsy in various physical activities?"

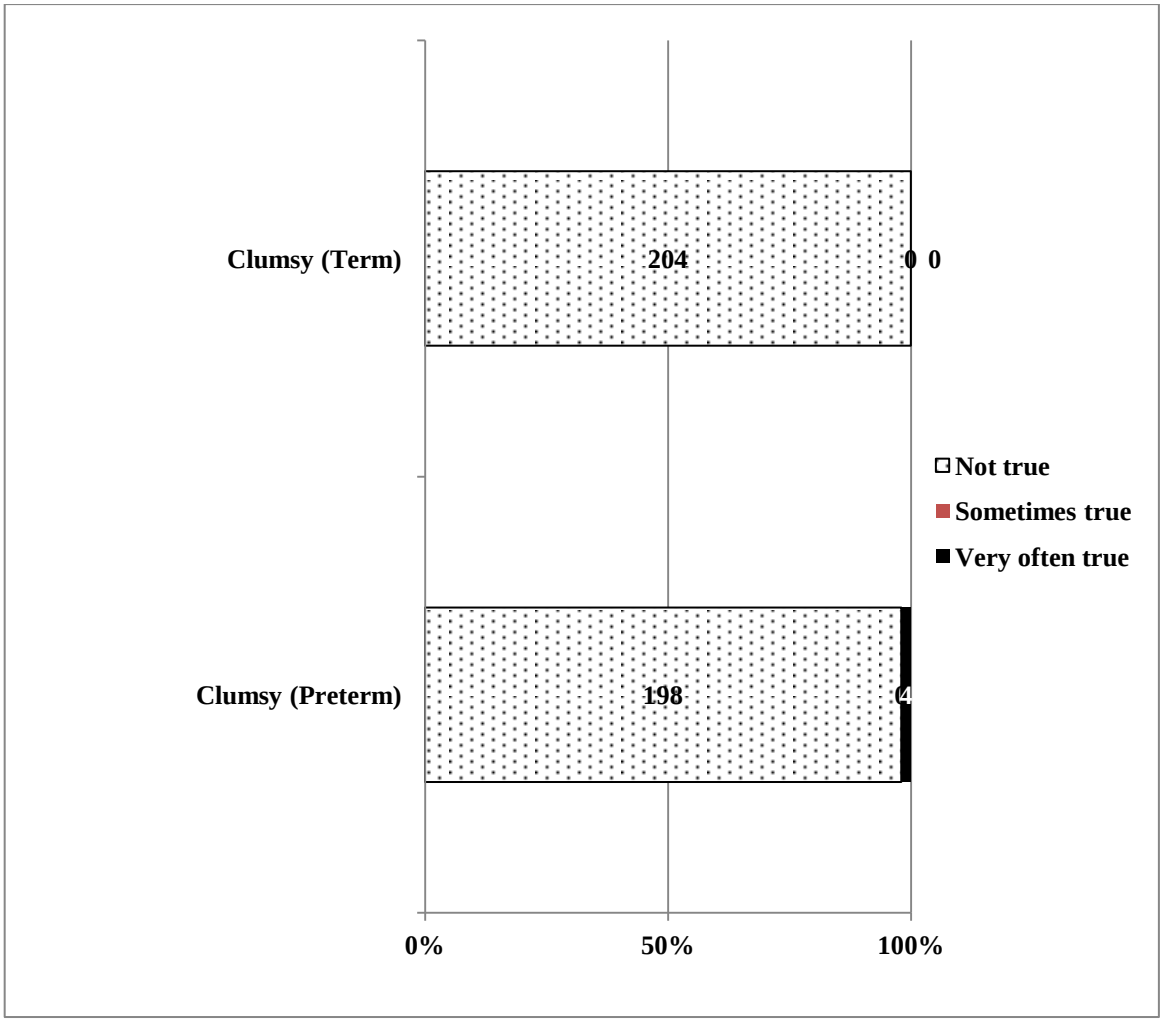


Table 7.29 Responses to the BIDS "Does he / she often prefer being with the younger children when compared to his age?"

BIDS question	Response	Preterm born		Term born	
		Freq	%	Freq	%
Prefers younger children	Not true	181	89.6	202	99.0
	Sometimes true	4	2.0	0	0
	Very true	17	8.4	2	1.0

Chi square value = 16.984, p < 0.000

Figure 7.12 Responses to the BIDS question "Does he / she often prefer being with the younger children when compared to his age?"

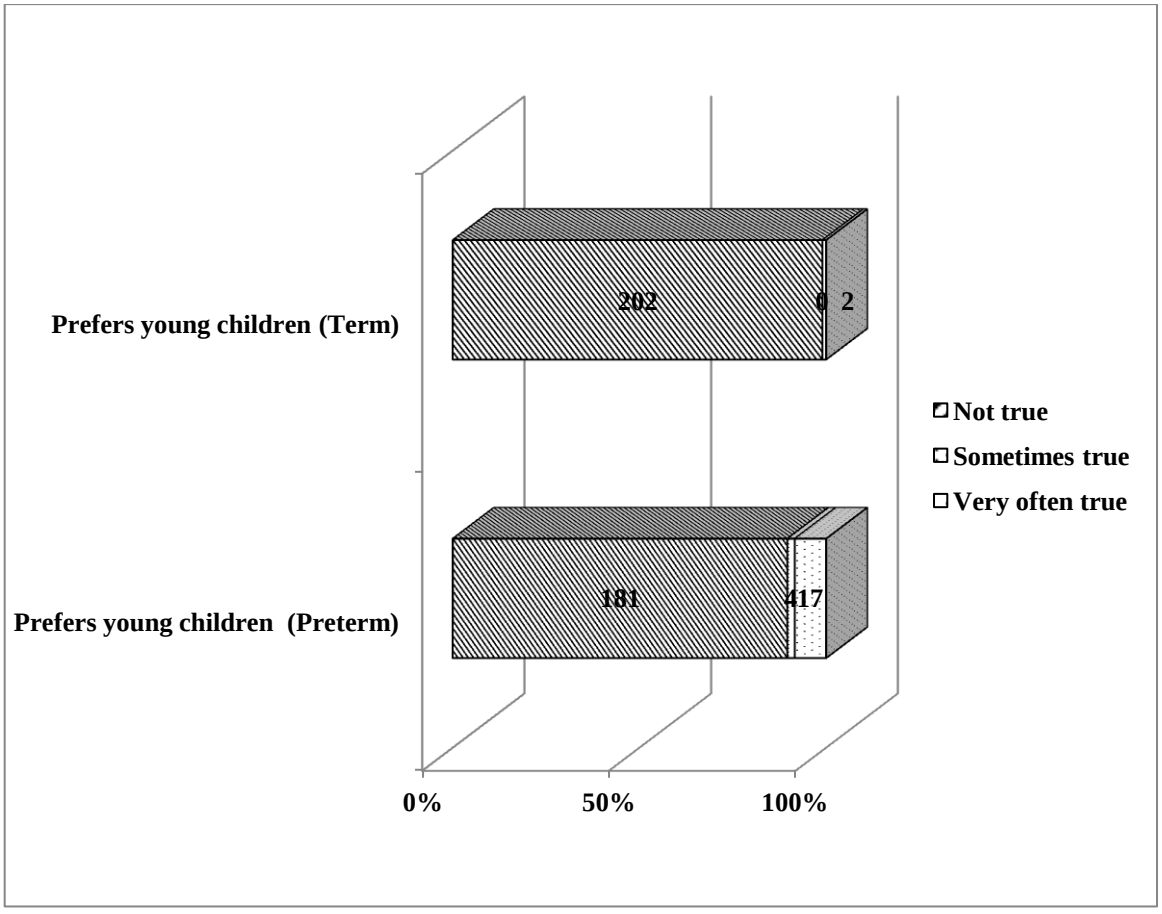


Table 7.30 Responses to the BIDS "Does he / she wet himself / herself during the day?"

BIDS question	Response	Preterm born		Term born	
		Freq	%	Freq	%
Wets during the day	Not true	177	87.6	184	90.0
	Sometimes true	8	4.0	8	3.9
	Very true	17	8.4	12	5.9

Chi square value = 0.988, p > 0.05

Figure 7.13 Responses to the BIDS question "Does he / she wet himself / herself during the day?"

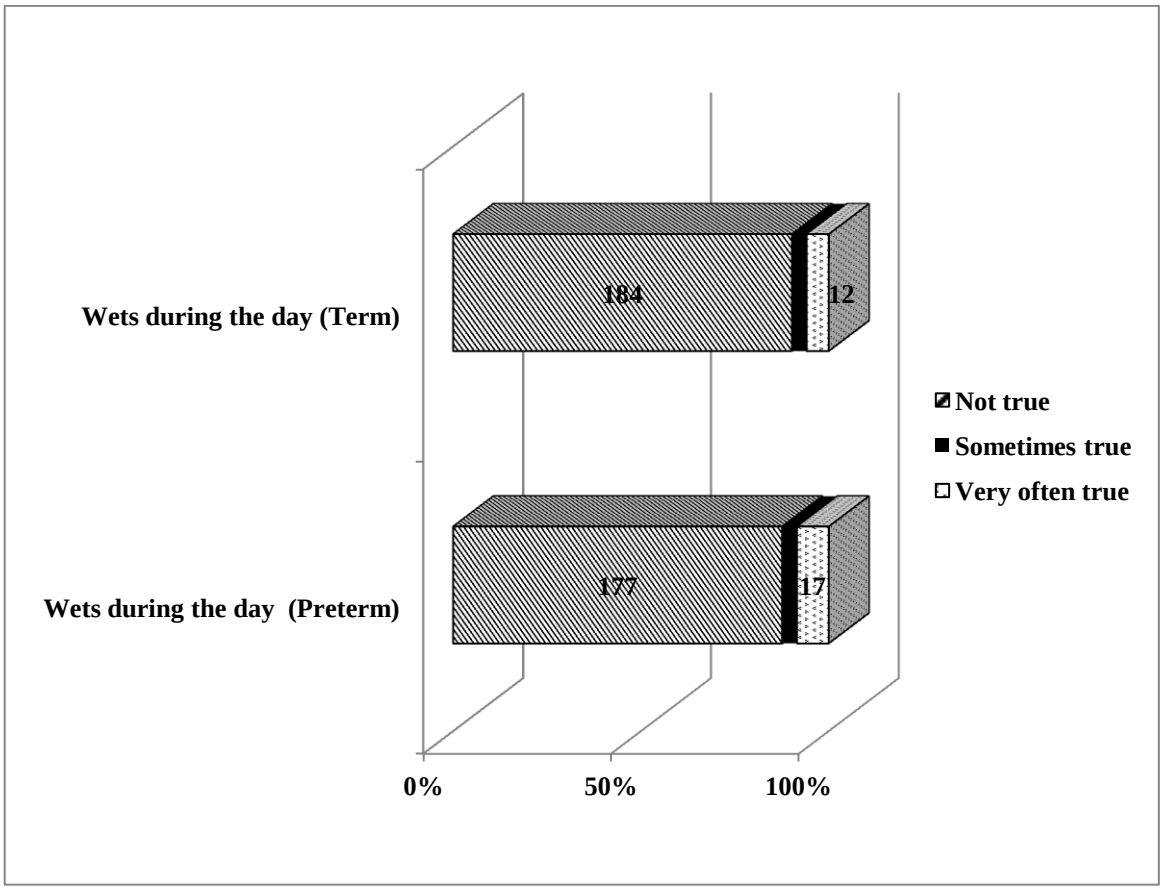


Table 7.31 Responses to the BIDS "Does he / she cling on to adults often or is very dependent on adults?"

BIDS question	Response	Preterm born		Term born	
		Freq	%	Freq	%
Clings or dependant	Not true	171	84.7	179	87.7
	Sometimes true	10	5.0	6	2.9
	Very true	21	10.4	19	9.3

Chi square value = 1.273, p > 0.05

Figure 7.14 Responses to the BIDS question BIDS "Does he / she cling on to adults often or is very dependent on adults?"

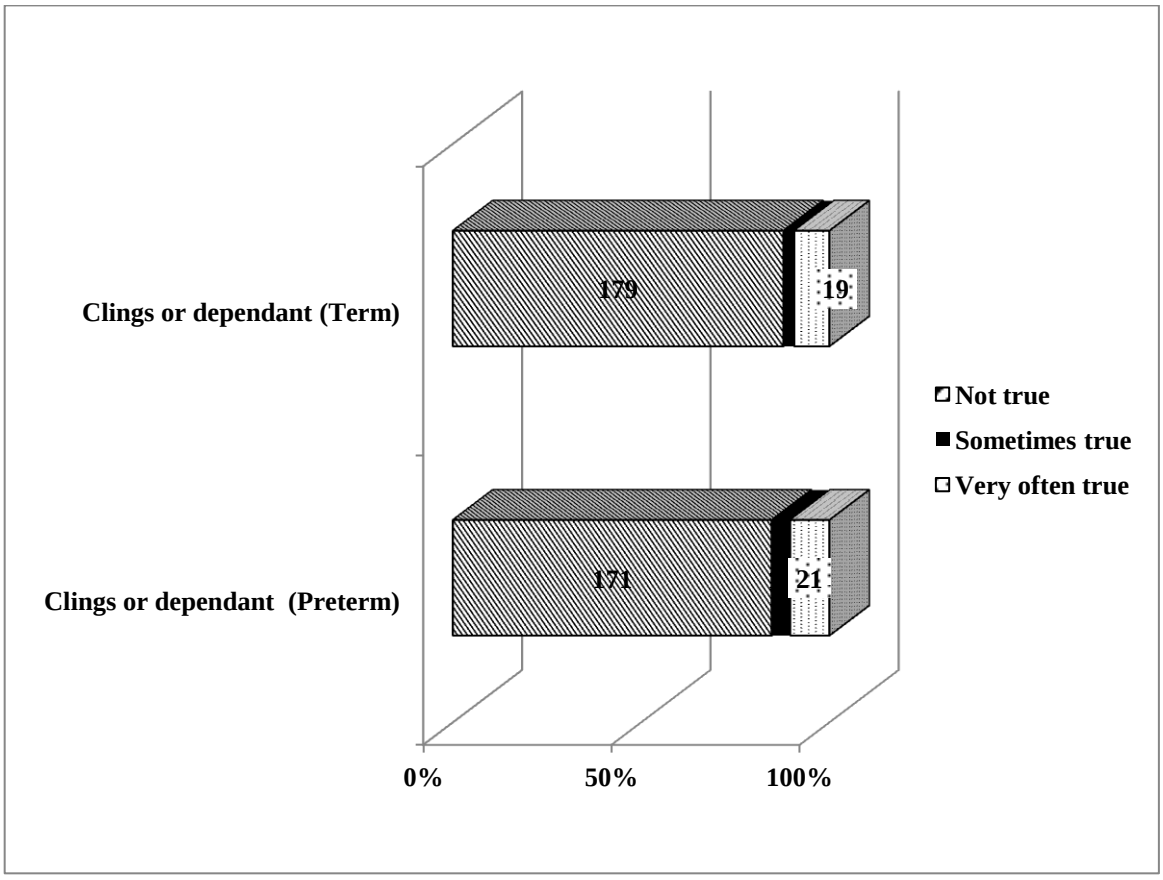
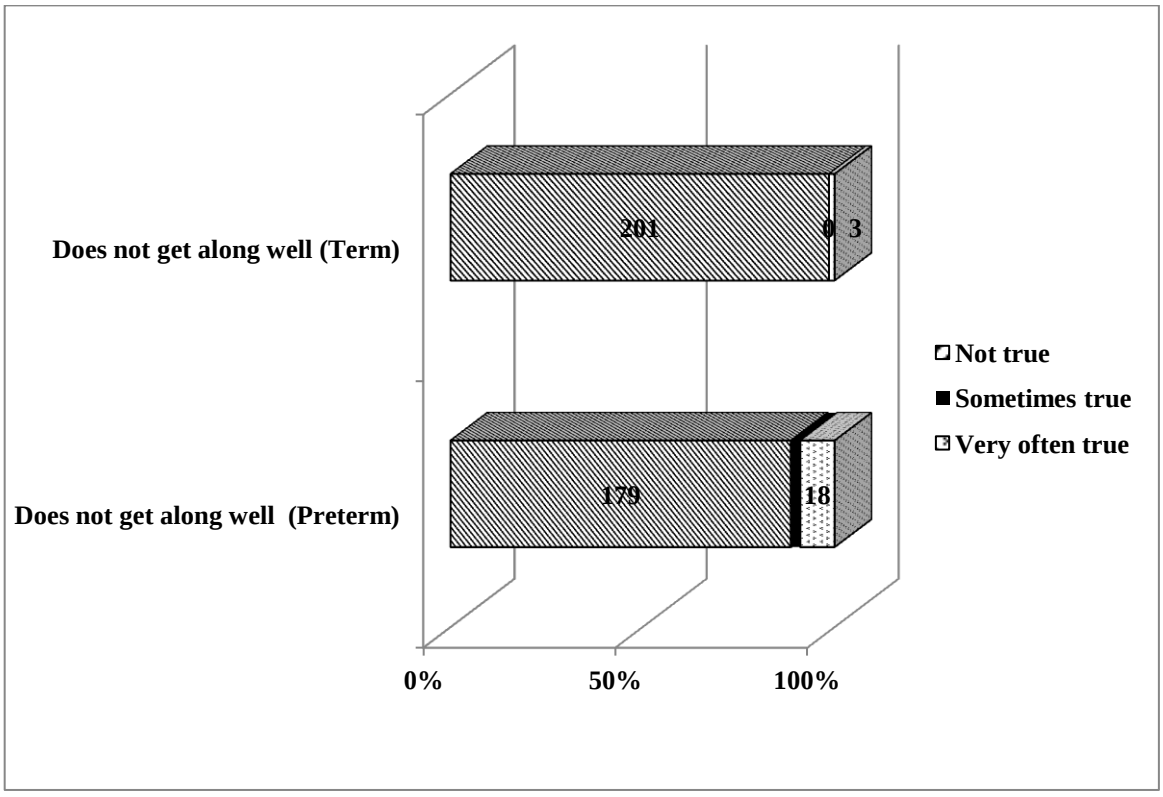


Table 7.32 Responses to the BIDS "Does he / she find it hard to get along well with the other children?"

BIDS question	Response	Preterm born		Term born	
		Freq	%	Freq	%
Does not get along well	Not true	179	88.6	201	98.5
	Sometimes true	5	2.5	0	0
	Very true	18	18.9	3	1.5

Chi square value = 16.979, p < 0.000

Figure 7.15 Responses to the BIDS question BIDS "Do he / she find it hard to get along well with the other children?"



There was a significant difference in the responses to the responses for individual questions between preterm and term born children for all the questions except 2 questions which were on – wets during the day and clings or dependant.

7.17 Relationship between various risk factors to BIDS scoring

An analysis of the various risk factors to the BIDS scores of more than 5 and less than 11; and more than 11 was done.

7.17.1 Preterm birth and a BIDS score of more than 5 and and less than 11 and more than 11

59 (29.2%) of the children born by preterm birth had a BIDS score greater than 5 compared to 11 (5.4%) of their term counterparts. There was a highly significant association between children being born preterm having a BIDS score of more than 5 (Chi square value = 40.346, $p < 0.05$) (Table 7.34). These screen-positive children were referred to Child and adolescent psychiatry for further evaluation.

11 (5.4%) of the children born by preterm birth had a BIDS score of more than 11 when compared to 1 (0.5%) of their term counterparts. There was a highly significant association between children being born preterm having a BIDS score of more than 11 (Fisher's exact <0.05) (Table 7.33).

These children along with their parents/care-giver were referred to Child and Adolescent psychiatry for counselling and management.

Table 7.33 Relationship between preterm birth and a BIDS score of more than 5 and less than 11 and more than 11

Preterm birth and BIDS score	More than or equal to 5	Less than 5	Total	More than or equal to 11	Less than 11	Total
Preterm born children	59 (29.2%)	143 (70.8%)	202	11 (5.4%)	191 (94.6%)	202
Term born children	11 (5.4%)	193 (94.6%)	204	1 (0.5%)	203 (99.5%)	204
Total	70	336	406	12	394	406
	Chi square value = 40.346, p = 0.000 RR = 5.417 (2.933 – 10.005)			***Fisher's exact = 0.003 RR = 11.109 (1.448 – 85.251)***		

The BIDS scores scored for the various gestational periods of preterm born children (as per the WHO classification) was compared with those of the term born children. There was an increasing trend seen with the number of children having higher BIDS scores of both >5 and >11 with a decreasing gestational age at birth among the preterm born children (Table 7.34 and 7.35).

There was a statistically significant difference in the BIDS scores, for both >5 and >11 among the various gestational classes of the preterm born children when compared to the term born children (Table 7.34 and 7.35).

Table 7.34 Relationship of BIDS score > 5 between preterm & term gestational ages

Gestational age – Preterm and Reference group (> 37 weeks)	BIDS score less than and more than 5 (n = 406)				RR	Chi-square	P value
	> 5		< 5				
	Freq	%	Freq	%			
Less than 28 weeks	2	40.0	3	60	**7.418 (2.195 – 25.069)**	**10.021**	**Fisher's = 0.032**
29 to 31 weeks	5	22.7	17	77.3	**5.058 (2.271 – 11.262)**	**17.600**	**0.000**
32 to 33 weeks	7	26.9	19	73.1	**5.706 (2.714 – 11.996)**	**24.606**	**0.000**
34 to 36 weeks	45	30.2	104	69.8	**5.601 (3.000 – 10.459)**	**39.707**	**0.000**
37 weeks and above	11	5.4	193	94.6	Reference group		
Total	**70**	**100**	**336**	**100**			

Table 7.35 Relationship of BIDS score of > 11 between preterm & term gestational ages

Gestational age – Preterm and Reference group (> 37 weeks)	BIDS score less than and more than 5 (n = 406)				RR	Chi-square	Fisher's exact
	> 11		<11				
	Freq	%	Freq	%			
Less than 28 weeks	1	20	4	80	**40.800 (2.953 – 563.7)**	**19.600**	**0.047**
29 to 31 weeks	0	0	22	100	**12.364 (1.153 – 132.53)**	**13.097**	**0.052**
32 to 33 weeks	2	7.7	24	92.3	**15.692 (1.675 – 146.97)**	**10.490**	**0.014**
34 to 36 weeks	8	5.3	141	94.7	**10.953 (1.385 – 86.636)**	**11.0518**	**0.005**
37 weeks and above	1	0.5	203	99.5	**Reference group**		
Total	**12**	**100**	**394**	**100**			

7.17.2 Consanguinity of parents and BIDS scores

Among the children who had parents who were consanguinously married, 31 (20.8%) BIDS score more than 5. There was no significant association between consanguinity and a BIDS score of more than 5 (Chi square = 2.095, p >0.05).

Among the children who had parents who were consanguinously married, 8 (5.4%) had a BIDS score more than 11. There was a significant association between the children having a BIDS score more than 11 (intellectually disabled) and their parents being consanguineously married) (Fisher's exact < 0.05) (Table 7.36)

Table 7.36 Relationship between consanguinity of parents and a BIDS scores

Consanguinity of parents BIDS score	More than or equal to 5	Less than 5	Total	More than or equal to 11	Less than 11	Total
Consanguinous	31 (20.8%)	118 (79.2%)	149	8 (5.4%)	141 (94.6%)	149
Non-consanguinous	39 (15.2%)	218 (84.8%)	257	4 (1.6%)	253 (98.4%)	257
Total	70	336	406	12	394	406
	Chi square value = 2.095, p > 0.05 RR = 1.371 (0.895 – 2.100)			***Fisher's exact = 0.036 RR = 3.450 (1.057 – 11.262)***		

7.17.3 Medical history for the mother when pregnant for the study child and BIDS scores

Among the mothers with an underlying medical condition, 2 mothers (14.3%) and 1 mother (7.1%) had children with a BIDS score more than 5 and more than 11respectively, and there was no significant association between a BIDS score of both more than 5 and 11 with the same (Fisher's exact > 0.05) (Table 7.37).

Table 7.37 Relationship between underlying medical condition for the mother and BIDS scores

Medical condition for mother and BIDS score	More than or equal to 5	Less than 5	Total	More than or equal to 11	Less than 11	Total
Present	2 (14.3%)	12 (85.7%)	14	1 (7.1%)	13 (92.9%)	14
Absent	68 (17.3%)	324 (82.7%)	392	11 (2.8%)	381 (97.2%)	392
Total	70	336	406	12	394	406
	Fisher's exact > 0.05 *RR = 0.824 (0.224 – 3.025)*			*Fisher's exact > 0.05* *RR = 2.545 (0.353 – 18.371)*		

7.17.4 Antenatal risk factor for the mother when pregnant for the study child and BIDS scores

Among the mothers who had an antenatal risk factor when she was pregnant for the study child, 6 children (26.1%) and 2 children (8.7%) had BIDS scores of more than 5 more than 11 respectively. However there was no significant association between the presence of an antenatal risk factor and the scores of more than 5 and 11 respectively (Table 7.38)

Table 7.38 Relationship between antenatal risk factor for the mother when pregnant for the study child and BIDS scores

Mother antenatal risk factor and BIDS score	More than or equal to 5	Less than 5	Total	More than or equal to 11	Less than 11	Total
Present	6 (26.1%)	17 (73.9%)	23	2 (8.7%)	21 (91.3%)	23
Absent	64 (16.7%)	319 (83.3%)	383	10 (2.6%)	373 (97.4%)	383
Total	70	336	406	12	394	406
	Chi square value = 1.337, p > 0.05 RR = 1.561 (0.757 – 3.218)			*Fisher's exact > 0.05 RR = 3.330 (0.774 – 14.322)*		

7.17.5 Family history of intellectual disability and BIDS scores

Among the children who had a family history of intellectual disability, 2 (10.5%) had a BIDS score more than 5.There was no children with a family history of intellectual disability and having a BIDS score of more than 11. There was no significant association between the presence of a family history of intellectual disability and having a score of more than 5 and 11 respectively (Fisher's exact > 0.05) (Table 7.39).

Table 7.39 Relationship between family history of intellectual disability and BIDS scores

Family history of intellectual disability and BIDS score	More than or equal to 5	Less than 5	Total	More than or equal to 11	Less than 11	Total
Present	2 (10.5%)	17 (89.5%)	19	0 (0%)	19 (100%)	19
Absent	68 (17.6%)	319 (82.4%)	387	12 (3.1%)	375 (96.9%)	387
Total	70	336	406	12	394	406
	Fisher's exact > 0.05 *RR = 0.599 (0.159 – 2.262)*			*Fisher's exact > 0.05* *RR = 1.032 (1.014 – 1.051)*		

7.17.6 Presence of a sibling with intellectual disability and BIDS scores

Those children who had a sibling with intellectual disability, 2 (20.0%) had BIDS scores of more than 5.There were no children with a BIDS score more than 11 and having an intellectually disabled sibling. There was no significant association between the presence of a sibling with intellectual disability and a BIDS score of more than 5 and 11 respectively (Table 7.45). BIDS score of more than 5.There were no children with a BIDS score more than 11 and having an intellectually disabled sibling. There was no significant association between the presence of a sibling with intellectual disability and a BIDS score of more than 5 and 11 respectively (Table 7.40).

Table 7.40 Relationship between presence of intellectual disability in the siblings and BIDS scores

History of intellectual disability in siblings and BIDS score	More than or equal to 5	Less than 5	Total	More than or equal to 11	Less than 11	Total
Present	2 (20.0%)	8 (80.0%)	10	0 (0%)	10 (100%)	10
Absent	68 (17.2%)	328 (82.8%)	396	12 (300%)	384 (97.0%)	396
Total	70	336	406	12	394	406
	Fisher's exact > 0.05 RR = 1.165 (0.331 – 4.099)			*Fisher's exact > 0.05 RR = 1.031 (1.013 – 1.049)*		

7.17.7 Not cried at birth and BIDS scores

Among the children who did not cry at birth there were 4 (55.6%) and 4 (44.4%) with BIDS scores of more than 5 and 11 respectively. There was a significant association between the child not having cried at birth and having a BIDS score of more than 5 and 11 respectively (Fisher's exact < 0.05) (Table 7.41).

Table 7.41 Relationship between the study child not having cried at birth and BIDS scores

Not cried at birth and BIDS score	More than or equal to 5	Less than 5	Total	More than or equal to 11	Less than 11	Total
Not cried	5 (55.6%)	4 (44.4%)	9	4 (44.4%)	5 (55.6%)	9
Cried	65 (16.4%)	332 (83.6%)	397	8 (2.0%)	389 (98.0%)	397
Total	70	336	406	12	394	406
	Fisher's exact = 0.010 ***RR = 3.393 (1.816 – 6.341)***			***Fisher's exact = 0.000*** ***RR = 22.056 (8.097– 60.074)***		

7.17.8 Low monthly family income and BIDS scores

Among the children who had monthly family incomes of less than 5000 Rs, 44 (18.9%) and 7 (3.0%) had a BIDS score of more than 5 and 11 respectively. There was no significant association between low monthly family income and BIDS scores of more than 5 and 11 respectively (Table 7.42).

Table 7.42 Relationship between low monthly family income and BIDS scores

Low income and BIDS score	More than or equal to 5	Less than 5	Total	More than or equal to 11	Less than 11	Total
< 5000 Rs	44 (18.9%)	189 (81.1%)	233	7 (3.0%)	226 (97.0%)	233
> 5000 Rs	26 (15.0%)	147 (85.0%)	173	5 (2.9%)	168 (97.1%)	173
Total	70	336	406	12	394	406
	Chi square value = 1.034, p > 0.05 RR = 1.257 (0.807 – 1.957)			*Chi square value = 0.005, p > 0.05 RR = 1.039 (0.336 – 3.220)*		

7.17.9 Young age of the mother and BIDS score

Among the children with mothers who gave birth to them at less than 23 years of age, 43 (19.1%) and 8 (3.6%) had a BIDS score of more than 5 and 11 respectively. However there was no significant association between a young aged mother and BIDS score of more than 5 and 11 respectively (Table 7.43).

Table 7.43 Relationship between young age of the mother and BIDS scores

Young age of the mother and BIDS score	More than or equal to 5	Less than 5	Total	More than or equal to 11	Less than 11	Total
< 23 years	43 (19.1%)	178 (80.9%)	221	8 (3.6%)	213 (96.4%)	221
> 24 years	27 (14.2%)	158 (85.8%)	185	4 (2.2%)	181 (97.8%)	185
Total	70	336	406	12	394	406
	Chi square value = 1.669, p > 0.05 RR = 1.333 (0.859 – 2.070)			*Fisher's exact > 0.05 RR = 1.674 (0.512 – 5.472)*		

7.17.10 Low socioeconomic status and BIDS scores

Among the children who belonged to the lower and upper lower socioeconomic class, 46 (18.6%) and 9 (3.6%) had a BIDS scores of more than 5 and 11 respectively. However there was no significant association between a low socioeconomic status and BIDS scores of more than 5 and 11 respectively (Table 7.44).

Table 7.44 Relationship between low socioeconomic status and BIDS scores

Low SES and BIDS score	More than or equal to 5	Less than 5	Total	More than or equal to 11	Less than 11	Total
Lower and upper lower	46 (18.6%)	201 (81.4%)	247	9 (3.6%)	238 (96.4%)	247
Lower middle and upper middle	24 (15.1%)	135 (84.9%)	159	3 (1.9%)	156 (98.1%)	159
Total	70	336	406	12	394	406
	Chi square value = 0.844, p > 0.05 RR = 1.234 (0.786 – 1.938)			*Fisher's exact > 0.05 RR = 1.931 (0.531 – 7.025)*		

7.17.11 Anaemia and BIDS score

Among the children who had mothers who were anaemic during their pregnancy for the participant, 18 (20.0%) and 1 (1.1%) had BIDS scores of 5 and 11 respectively. There was however no significant association between anaemia and the BIDS scores (Table 7.45).

Table 7.45 Relationship between anaemia in the mother during pregnancy and BIDS scores

Anaemia and BIDS score	More than or equal to 5	Less than 5	Total	More than or equal to 11	Less than 11	Total
Present	18 (20.0%)	72 (80.0%)	90	1 (1.1%)	89 (98.9%)	90
Absent	13 (13.4%)	84 (86.6%)	97	0 (0%)	97 (100%)	97
Total	31	156	187	1	186	187
	Chi square value = 1.470, p > 0.05 RR = 1.492 (0.777 – 2.868)			*Fisher's exact > 0.05 RR = 0.989 (0.967 – 1.011)*		

7.17.12 Fewer antenatal visits and BIDS scores

Among the children with mothers had less than 4 antenatal visits during their pregnancy, 12 (26.7%) and 1(2.2%) had BIDS scores of more than 5 and 11respectively. For those with a score of more than 5 there was a narrow miss in the significance with antenatal visits (Chi square = 1.470, p = 0.076). However, this was not true in the case of those with a score of more than 11 (Table 7.46).

Table 7.46 Relationship between less than 4 ANCs for the mother during pregnancy and BIDS scores

Less than 4 ANCs and BIDS score	More than or equal to 5	Less than 5	Total	More than or equal to 11	Less than 11	Total
Present	12 (26.7%)	33 (73.3%)	45	1 (2.2%)	44 (97.8%)	45
Absent	58 (16.1%)	303 (83.9%)	361	11 (3.0%)	350 (97.0%)	361
Total	70	336	406	12	394	406
	Chi square value = 3.151, p = 0.076 RR = 1.660 (0.968 – 2.845)			*Fisher's exact > 0.05 RR = 0.729 (0.096 – 5.517)*		

12 (26.7%) and 1(2.2%) had BIDS scores of more than 5 and 11respectively. For those with a score of more than 5 there was a narrow miss in the significance with antenatal visits (Chi square = 1.470, p = 0.076). However, this was not true in the case of those with a score of more than 11 (Table 7.51). Table 7.52 and 7.53 summarises various risk factors with a BIDS score of more than 5, less than 11 and more than 11.

Table 7.47 and 7.48 summarises various risk factors with a BIDS score of more than 5, less than 11 and more than 11.

Table 7.47 Summary of bivariate analysis of various risk factors with a BIDS score of more than 5 and less than 11

Sl No.	Risk factor	Chi Square	p value	RR (95% CI)
1.	Preterm birth	40.346	**0.000**	5.417 (3.671 – 14.275)
2.	Consanguinous marriage of parents	2.095	0.163	1.371 (0.895 – 2.100)
3.	Mother with medical condition	0.089	0.766	0.824 (0.224 – 3.025)
4.	Antenatal risk factor	1.337	0.248	1.561 (0.757 – 3.218)
5.	Family history of intellectual disability	-	Fisher's =0.549	0.599 (0.159 – 2.262)
6.	Siblings with intellectual disability	-	Fisher's =0.685	1.165 (0.331 – 4.099)
7.	Not having cried at birth		**Fisher's = 0.010**	3.393 (1.816 – 6.341)
8.	Income < Rs 5000	1.034	0.309	1.257 (0.807 – 1.957)
9.	Age of mother at birth < 23 yrs	1.698	0.192	1.344 (0.858 – 2.103)
10.	Low SES	0.844	0.358	1.234 (0.786 – 1.938)
11.	Anaemia in mother during pregnancy	1.470	0.225	1.492 (0.777– 2.868)
12.	Antenatal check-ups less than 4	3.151	0.076	1.660 (0.968 – 2.845)

Table 7.48 Summary of bivariate analysis of various risk factors with a BIDS score of more than 11

Sl No.	Risk factor	Chi Square	p value	OR (95% CI)
1.	Preterm birth	-	**Fisher's = 0.003**	11.109 (1.495 – 91.419)
2.	Consanguinous marriage of parents	-	**Fisher's 0.036**	3.450 (1.062 – 12.128)
3.	Mother with medical history	-	Fisher's =0.348	2.545 (0.320 – 18.371)
4.	Antenatal risk factor	-	Fisher's =0.143	3.330 (0.774 – 14.322)
5.	Family history of intellectual disability	-	Fisher's =1.0	1.032 (1.014 – 1.051)
6.	Siblings with intellectual disability	-	Fisher's =1.0	1.031 (1.013 – 1.049)
7.	Not having cried at birth	-	**Fisher's = 0.000**	22.056 (8.097 – 60.074)
8.	Income < Rs 5000	0.005	0.946	1.039 (0.336 – 3.220)
9.	Age of mother at birth < 23 yrs	-	Fisher's = 0.559	1.664 (0.509 – 5.436)
10.	Low SES	-	Fisher's = 0.380	1.931 (0.531 – 7.025)
11.	Anaemia in mother during pregnancy	-	Fisher's = 0.481	0.989 (0.967 – 1.011)
12.	Antenatal check-ups less than 4	-	Fisher's = 1.0	0.729 (0.096 – 5.517)

7.18 Multivariate analysis to examine associations between 'BIDS score (>5) on preterm birth' and its various risk factors

A binary logistic regression was performed to view the effect of Preterm birth, not having cried at birth, consanguinity and antenatal visits less than 4 on the BIDS score of more than 5. After adjusting for the possible confounding factors it was found that the relative risk of a child born by preterm birth having a Brief Intellectual Disability (BIDS) score more than 5 that is being screen positive for intellectual disability was 6.732 times when compared to the children born term ($p < 0.05$) (Table 7.49).

Table 7.49 Multivariate analysis of the outcome 'BIDS score (> 5) on preterm birth' and its various risk factors, using binary logistic regression

Sl No	Variables in the model	RR (95% CI)	p value
1	Preterm birth	**6.732 (3.394 – 13.353)**	**0.000**
2	Consanguinity	1.256 (0.719 – 2.193)	0.423
3	Not cried at birth	3.033 (0.778 – 11.826)	0.110

7.19 Multivariate analysis to examine associations between 'BIDS score (>11) on preterm birth' and its various risk factors

Similarly a multivariate binary logistic regression was performed to view the effect of preterm birth, consanguinity and not having cried at birth and antenatal visits less than 4 on the BIDS score of more than 11. After adjusting for the possible confounding factors it was found that the relative risk of a child born by preterm birth having a Brief Intellectual Disability (BIDS) score more than 11, that is an intellectual disability was 7.204 times ($p = 0.058$) when compared to the children born by term birth (Table 7.50).

Table 7.50 Multivariate analysis of the outcome 'BIDS score (> 11) on preterm birth' and its various risk factors, using binary logistic regression

Sl No	Variables in the model	RR (95% CI)	p value
1	Preterm birth	**7.204 (0.875 – 59.303)**	**0.058**
2	Consanguinity	2.583 (0.705 – 9.464)	0.152
3	Not cried at birth	**17.888 (3.799 – 84.218)**	**0.000**

8. Discussion

This study aims to elucidate the role of preterm birth on the intellectual disability. However it is important to examine the study population to elicit differences between the preterm and term born children which may confound the relationship between preterm delivery and intellectual disability.

There were more number of males (54.5%) than females (45.5%) among the preterm born children whereas in the term born group, females (52.5%) were more than males (47.5%). It is usually the male child who is at a higher risk of complications and death at birth but this was not demonstrated in our study. (96)

28 children were taken care of by caregivers other than mother or father (20 children born by preterm birth and 8 children born by term birth). There were more preterm children being taken care of caregivers other than parents when compared to the term born children. This is important since the primary caregiver could potentially have an influence on the holistic growth of a child. (97) A primary caregiver other than father or mother may not have a positive role especially in the preterm born children with intellectual disability. Primary caregivers other than parents may not adequately address the emotional needs of the child as compared to parents who are more inclined to the emotional needs of the child and always willing to take additional steps for "my child" which is not the case in caregivers other than parents. Grandparents may be an exception to this (97). This is important since in our study aunts were the main caregivers for the preterm children and this could potentially be a factor in the development of intellectual disability among these preterm born children.

A vast majority of the parents in both the preterm and term children group had attended upto middle school. There were more parents without formal education among the

preterm group (19.8%) when compared to the term group. (10.3%) Parents with low education not only face challenges in coping with intellectually disabled child but fail to understand the sensitivity of the problem. (98) (99)

Majority of both the preterm and term born group of children were from families that engaged themselves in semi-skilled occupation and most of them had a family incomes between Rs 1744 – 5223. 78.2% of the preterm born children and 76.5% of the term born children were from families who belonged to the upper lower class. Preterm births are strongly associated with those coming from a lower education and socioeconomic background. (39) This can be a major factor in not just determining preterm birth but also the later aftermaths of preterm birth, the major one being defects in cognition and intellectual disability. Parents from a lower education and socioeconomic background may fail to understand the special needs and emotions of an intellectually disabled child if present in their family. (12) (98)

57.4% of the preterm born children and 55.9% of the term born children had mothers who were married at less than 19 years of age. Mothers who were married early tend to deliver early. Their young age makes the mother unable to face the consequences of preterm birth. (37) Conganguinous marriages are a common practice in Kaniyambadi block and this was seen in the study with a prevalence rate of 37%. Mumtaz B et al. has shown a strong association between consanguinity and preterm birth. (100) Among the consanguinous marriages, 74% were third degree consanguineous marriage and 26% were second degree consanguineous marriages. Our study however did not find any association between consanguinous marriage and preterm birth nor intellectual disability.

11 (5.4%) of the preterm born children and 16 (7.8%) of the term born had parents who had a history of primary infertility (for more than 5 years). There were more children born

term, whose parents had a history of primary infertility. Though there was no association in the present study between preterm birth and infertility, Goldberg et al has shown such an association especially in those who have taken treatment for infertility. (37)

11 (5.4%) of the mothers of preterm born children and 3 (1.5%) of the mothers of term born had an associated medical condition present prior to the birth of the child. The predominant medical condition among these mothers was Diabetes mellitus for both who delivered term and preterm babies. There were more diabetic and hypertensive mothers among the preterm born children than the term born. Among the preterm born children, 15 (7.4%) of their mothers had an underlying antenatal risk factor for that pregnancy when compared to the term born children who had 8 (3.9%) of their mothers having the same. The predominant antenatal risk factors in the mothers with preterm born children were Pre-eclampsia / eclampsia and twin pregnancy. The main reason could be systemic inflammation triggered by the presence of Diabetes or pre-eclampsia. (37) Hence it may become necessary in the proper management of these conditions in pregnancy to avoid preterm birth and thereby reducing the burden of intellectual disability among the preterm born children.

Mothers of preterm born children had fewer antenatal visits when compared to their term counterparts. However this may be a spurious association because mothers who have had preterm deliveries would very obviously tend to have had fewer antenatal visits when compared to their term counterparts as a direct consequence of labour. The antenatal visits in early pregnancy are fewer (once in 4 – 6 weeks) when compared to frequent antenatal visits in late pregnancy (Once in 1 – 2 weeks) (37).

8 (4.0%) of the preterm born children had a family history of intellectual disability when compared to 11 (5.4%) of the term born, mainly being cousins. 8 (4.0%) of the preterm

born children and 2 (1.0%) of the term born children had a sibling with intellectual disability. 40 (47.6%) of the mothers with preterm born children and 50 (48.5%) of the mothers with term born children were anaemic (PCV < 33.0%). Maternal nutritional status was an important factor influencing preterm birth and thereby its consequences. (37)

CHAD hospital was the commonest place of delivery among both preterm and term born children (59.4% of preterm born children and 59.85 of the term born children). This was because CHAD hospital historically has offered maternal and child health services to the population of Kaniyambadi block. 40 (19.8%) preterm born children delivered at home. There were more breech extractions and LSCS among the preterm born (2.5% and 9.9% respectively) when compared with the term born (0.5% and 6.3% respectively).

Among the 202 preterm children, 9 (4.5%) of the children did not cry. All term born children cried at birth. In our study there was significant association between a baby not crying at birth and development of intellectual disability subsequently later in life, similar to the findings in the Danish study by Ehrenstein et al. (101). In our study there was a 17.8 times risk of a child developing intellectual disability if the child had not cries at birth.

Majority of the preterm born children 149 (73.8%) were late preterms. The remaining was constituted by 26 (12.9%) moderate preterms and 24 (11.9%) severe preterms. There were 3 (1.5%) preterms who were born extremely preterm. There were more numbers of low birth weight, very low birth weight and extremely low birth weight among the preterm born children when compared to the term born children. Overall there was a significant association between presence of a medical condition in the mother, less than 4 antenatal visits and the presence of a sibling with a history of intellectual disability with

preterm birth,. These risk factors were considered as important risk factors indirectly influencing intellectual disability in the children born by preterm birth.

There was a significant difference in the responses to the responses for individual questions of the BIDS questionnaire between preterm and term born children for all the questions except two questions which were on – wets during the day and clings or dependant. The risk of a preterm child being suspected to have a probable intellectual disability (BIDS score > 5) was more than 6 times when compared to a term born child. The risk of a preterm born child developing definitive intellectual disability was 11 times when compared to that of a term born child. This was much higher as stated in the review by Farin et al which in which studies showed a 3 times increased risk in intellectual disability among children born prematurely. (102). Our study showed an incidence of 5.4% of intellectual disability among the preterm born children, whereas the Danish study done by Mathiasen et al showed an incidence of 11.5%. (46) The Danish study may show greater intellectual disability because preterm born children have a better survival in the developed countries compared to the developing world .However the increased survival of the severely preterm children is associated with increased intellectual disability in the survivors..

There was no dose response relationship seen between gestational age and intellectual disability.This is probably because of the death of severely preterm . This is contrary to the study by Kerr-Wilson et all where a dose-response relationship was deduced where it was observed in the form of falling scores of intelligent quotient with a decreasing gestational age. (103) An ethical dilemma emerges in the developing world whether it is actually worthwhile in investing in the enormously expensive intensive neonatal care of the severely preterm born babies since firstly, their survival rates in the developing regions are low and even if they do make it there is always a high chance of residual

defects in cognition which further add to the economic and disability burden of the family as well as the nation.

Our study showed that apart from preterm birth, consanguinity of parents and the baby not having cried at birth showed a strong association with intellectual disability (BIDS score of more than 11), the risk being 3.4 times and 22 times respectively. This is important since these children if offered referral at the right time can be evaluated appropriately and managed accordingly if found to be intellectually disabled.

Overall, the incidence of intellectual disability among the preterm born children in Kaniyambadi block was 5.4% when compared to 0.49% in the term born children. This is a strong finding since a BIDS score of more than 11 has a specificity of 100%. Hence there was a definite reduction in the intellectual ability observed among the children born by preterm birth when compared to those born by term birth. There are not many studies to substantiate this in India except the Pune study by Chaudhari et al. that had findings which correlated with our study. They had however used low birth weight as the exposure factor for intellectual disability. The Pune study showed a 24.4% incidence of sub-normal intelligence in their study population of low birth weight children. (18) There have been no studies done in India on the intellectual disability of birth cohorts of preterm born children so far. Also there are many western studies done on the effects of low birth weight on cognition and IQ with very few on preterm born children.

9. Conclusions

1. The incidence of intellectual disability among the preterm children born in Kaniyambadi block was 5.4% compared to 0.49% among the term born children.
2. Preterm born children had 11 times greater risk of developing intellectual disability in comparison to the term born children.
3. 59 (29.2%) of the children born by preterm birth developed probable intellectual disability (BIDS score greater than 5) compared to 11 (5.4%) of their term counterparts.
4. Children born preterm had 6.732 times greater risk of developing probable intellectual disability compared to the children born term.

10. Recommendations

1. The study found a strong association between preterm birth and the child subsequently being intellectually disabled. It is therefore recommended to have early screening for intellectual disability using simple g tools like the Brief Intellectual Disability scale. It may be necessary to incorporate the screening tool at an early stage where the child has not yet made or is forced into career choices
2. It is recommended that efforts be taken to prevent preterm births.
3. Larger studies are needed to further understand the association of preterm birth with intellectual disability. Long term follow up of birth cohorts from national registries is ideal to study the effect of preterm birth on intellectual disability.

11. Limitations

1. Interviewer bias: The interviewer was not blinded to the preterm or term born status of the children in the study.
2. Information bias: The intellectual problems present in the preterm children might have been understated by the parent or the caregiver especially in situations where there is a close relative or friend in the vicinity of the interview to avoid unpleasant situations that the child or the family might face later.
3. Unknown last menstrual periods and irregular cycles might have influenced the gestational ages especially in the borderline preterm born children.

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13. Annexure

Annexure I: Performa for data collection:

Effect of Pre-term birth on Intellectual Ability– A community based non-concurrent cohort study in South India (EPIAS study)

Department of Community Health And Development, Christian medical college, Vellore, Tamil Nadu

Questionnaire

1. Serial Number: _____
2. Study Participant number: _____
3. Name of the participant: _____
4. Date of Birth: __/__/__
5. Age in completed years: ____
6. Sex: Male / Female
7. Address for communication:

   _____

   _____

   _____
8. Phone number: _____
9. Name of the father: _____
10. Current age of the father in years: ____
11. Name of the mother: _____
12. Current age of the mother in years: ____
13. Name of the caregiver (if other than father/mother): _____
14. Current age of the caregiver in years: ____

Socio-Demographic details:

1. Education :

   - Illiterate □
   - Primary school certificate □
   - Middle school certificate □
   - High school certificate □
   - Intermediate or post-high school diploma □
   - Graduate or post-graduate □

- Profession or honours □

2. Occupation :
   - Profession □
   - Semi-profession □
   - Clerical/Shop-owner/Farmer □
   - Skilled □
   - Semi-skilled □
   - Unskilled □
   - Unemployed □

3. Income (Rs): _____
   - ≤ 1743 □
   - 1744-5223 □
   - 5224-8706 □
   - 8707-13028 □
   - 13029-17414 □
   - 17415-34829 □
   - ≥ 34830 □

4. Total SES score *(Kuppuswamy's Socio-economic Status Scale-Updating Income Ranges for the Year 2013) :* _____

Antenatal history:

1. Age of mother at marriage (in years): ____
2. Age of father at marriage (in years): ____
3. Was the marriage:
   - Consanguinous □
   - Non-consanguinous □

   If consanguinous, degree of consanguinity:

   - First degree □
   - Second degree □
   - Third degree □
4. Any history of primary/secondary infertility for conceiving the study participant? Yes / No
   If yes, did you conceive after treatment for infertility? Yes / No
   If yes, after how many years of treatment: ____
5. Birth order of the study participant: ____
6. Any significant medical history for the mother? _____

7. Any bad obstetric history? Yes /
   No:_____
8. Any ante-natal risk factors? Yes / No
   If yes, what?
   - Pregnancy induced hypertension □
   - Pre-eclampsia / Eclampsia □
   - Gestational Diabetes mellitus □
   - Twin pregnancy □
   - Hypothyroidism □
   - Intrauterine growth retardation □
   - Placenta praevia □
   - TORCH infection □
   - Cardiac problems □
   - Bronchial Asthma □
   - Others: _____
9. Total number of antenatal visits you had for the study participant: _____
10. Where did you have these antenatal visits:
    - CHAD hospital □
    - CMCH □
    - Primary health centre □
    - GVMCH □
    - Private set-up □
    - Others: _____
11. Did you have any fever during pregnancy? Yes / No
12. Any history of drug usage during pregnancy? Yes / No
    If yes, which drug? _____
13. Is there a family history of intellectual disability or mental retardation? Yes / No
    If yes, who is the family member? _____
14. Do any of your other children suffer from problems of intellectual disability or mental retardation? Yes / No
    If yes, which child? _____

    <u>If Antenatal folder available, note the following:</u>
    a. Packed cell volume (PCV) / Haemoglobin level (Hb%): _____
    b. Blood group: _____
    c. VDRL status: Positive / Negative
    d. HBsAg status: Positive / Negative
    e. HIV status: Positive / Negative
    f. GTT/GCT: _____

<u>Birth details:</u>

1. Gestation (in weeks) at the time of delivery: _____

2. Place of delivery:
   - CHAD hospital □
   - CMCH □
   - Primary health centre □
   - GVMCH □
   - Private set-up □
   - Home delivery □
   - Others: _____
3. Mode of delivery:
   - Normal vaginal delivery □
   - Suction cup extraction □
   - Forceps extraction □
   - Breech extraction □
   - Lower segment caesarean section □
4. If lower segment caesarean section, what was the indication?
   _____
5. Did the baby cry at birth? Yes / No
6. Did the baby need any resuscitation soon after birth? Yes /No
7. APGAR details (if records available):
   APGAR at 1 minute: _____
   APGAR at 5 minutes: _____
8. Birth weight: ____kg
9. Head circumference: _____cm
10. Length: _____cm
11. Any history of seizures within 24 hours of birth? Yes / No
12. Was the baby hospitalised for more than 24 hours? Yes /No
    If yes, what was the indication?
    _____

Anthropometry

1. Height (standing): _____cm
2. Weight: _____kg
3. Mid-arm circumference: _____cm

Current medical history

1. Does your child suffer from any of the following:
   - Seizure disorder
   - Inborn error of metabolism
   - Cerebral palsy
   - Congenital heart disease

- Respiratory problems
- Endocrine disorders
- Others: _____
- None

2. Does your child suffer from frequent episodes of diarrhoea? Yes / No
   If yes, how often: _____times/week

Brief Intellectual Disability Scale (BIDS)

1. Does he / she act too young for his age?
   - Not true □
   - Somewhat or sometimes true □
   - Very true or often true □ Score: ___

2. Does he / she suffer from poor school work?
   - Not true □
   - Somewhat or sometimes true □
   - Very true or often true □ Score: ___

3. Does he / she suffer from speech problems?
   - Not true □
   - Somewhat or sometimes true □
   - Very true or often true □ Score: ___

4. Does he / she suffer from problems where it is difficult to concentrate or pay attention for too long?
   - Not true □
   - Somewhat or sometimes true □
   - Very true or often true □ Score: ___

5. Does he / she get often teased by the others?
   - Not true □
   - Somewhat or sometimes true □
   - Very true or often true □ Score: ___

6. Do he / she often prefer being with the younger children when compared to his age?
   - Not true □
   - Somewhat or sometimes true □
   - Very true or often true □ Score: ___

7. Is he poorly coordinated or clumsy in various physical activities?
    - Not true □
    - Somewhat or sometimes true □
    - Very true or often true □ Score: ___

8. Does he / she wet himself / herself during the day?
    - Not true □
    - Somewhat or sometimes true □
    - Very true or often true □ Score: ___

9. Does he / she clings on to adults often or is very dependent on adults?
    - Not true □
    - Somewhat or sometimes true □
    - Very true or often true □ Score: ___

10. Does he / she find it hard to get along well with the other children?
    - Not true □
    - Somewhat or sometimes true □
    - Very true or often true □ Score: ___

BIDS scoring

Not true = 0

Somewhat or sometimes true = 1

Very true or often true = 2

Total BIDS score: _____

Questionnaire administered by:
Signature:
Date:
Time:
Place:
Has the child been referred for further evaluation to the department of child and adolescent psychiatry: Yes / No

Annexure II: Kuppusamy's scale (Original classification), modified in 2013

	Score
Education	
Profession or honours	7
Graduate or post graduate	6
Intermediate or post high school diploma	5
High school certificate	4
Middle school certificate	3
Primary school certificate	2
Illiterate	1
Occupation	
Profession	10
Semi-profession	6
Clerical, shop-owner, farmer	5
Skilled worker	4
Semi-skilled worker	3
Unskilled worker	2
Unemployed	1
Family income per month (in Rs.)	
≥2000	12
1000-1999	10
750-999	6
500-749	4
300-499	3
101-299	2
≤100	1
Socioeconomic class	
Upper	26-29
Upper middle	16-25
Lower middle	11-15
Upper lower	5-10
Lower	0<5

	Score
Education	
Profession or honours	7
Graduate or post graduate	6
Intermediate or post high school diploma	5
High school certificate	4
Middle school certificate	3
Primary school certificate	2
Illiterate	1
Occupation	
Profession	10
Semi-profession	6
Clerical, shop-owner, farmer	5
Skilled worker	4
Semi-skilled worker	3
Unskilled worker	2
Unemployed	1
Family income per month (in Rs.)	
≥2000	12
1000-1999	10
750-999	6
500-749	4
300-499	3
101-299	2
≤100	1
Socioeconomic class	
Upper	26-29
Upper middle	16-25
Lower middle	11-15
Upper lower	5-10
Lower	0<5

Monthly family income, amended with reference to change in the consumer price indices till 2013

Monthly Family Income	Score
<1743	1
1744 - 5223	2
5224 - 8706	3
8707 – 13,028	4
13,029 – 17,414	6
17,415 – 34,829	10
>34,830	12

Annexure III: Written informed consent document to participate in the EPIAS (Effect of Preterm birth on Intellectual Ability South India) study

Study Title: Effect of pre-term birth on Intellectual ability – A community based non-concurrent cohort study in South India

Serial Number: _____

Study Number: _____

Subject's Name: _____

Name of the Parent/Guardian/Caregiver: _____

Phone Number: _____

Address: _____

Date of Birth / Age (participant): _____

Date of Birth / Age (Parent / Guardian / Caregiver): _____

_____

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions.

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

(iii) I understand that the Investigators of the study will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

(v) I agree to take part in the above study.

Contact details:

Dr Chella Sindhu KN

Department of Community health and development.

Christian Medical College,

Vellore, Tamil Nadu,

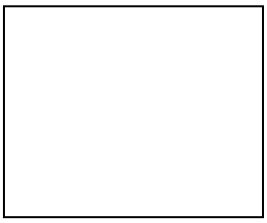
India – 632002.

Ph: 9994325172

Signature (or Thumb impression) of the Subject's parent/guardian/caregiver:

Signatory's Name: _____

Signature: _____

Or  (Left Thumb impression)

Date: _____/_____/_____

Signature of the Investigator: _____

Study Investigator's Name: _____

Date: _____/_____/_____

Signature or thumb impression of the Witness: _____

Name & Address of the Witness: _____

_____

Date: _____/_____/_____

Annexure IV: Facsimile of Informed consent document - Tamil

<u>ஆய்வில் பங்கேற்பதற்கான தெரிவிக்க பட்ட ஒப்புதல் படிவம்</u>:

குறைமாதப்பிறப்பு , அறிவுத்திறன் மீது ஏற்படுத்தும் தாக்கம் - *(EPIAS) ஆய்வு*:

ஆய்வின் தலைப்பு: குறைமாதப்பிறப்பு , அறிவுத்திறன் மீது ஏற்படுத்தும் தாக்கம் -- தென் இந்தியாவில் நடத்தப்படும் சமூகக்குழும ஆய்வு.

வரிசை எண்:----------

ஆய்வு எண்: ----------

பங்கேற்பவரின் பெயர்: ----------

பெற்றோர்/ காப்பாளர்/ பாதுகாவலர் பெயர்: ----------

தொலைபேசி எண்: ----------

முகவரி: ----------

பிறந்த தேதி/ வயது (பங்கேற்பவர்): ----------

பிறந்த தேதி/ வயது (பெற்றோர்/ காப்பாளர்/ பாதுகாவலர்):

i) ---------- தேதி இட்ட தகவல் படிவத்தை நன்கு படித்து நான் புரிந்து கொண்டேன். மேலும் எனது சந்தேகங்களை கேட்டு தெரிந்துகொள்ள எனக்கு வாய்ப்பு தரப்பட்டது.

ii) நான் இந்த ஆய்வில் பங்கேற்பது எனது தன்னார்வத்தால் என்றும், எப்பொழுது வேண்டுமானாலும் நான் இந்த ஆய்வில் இருந்து விலகிக்கொள்ளலாம் என்றும் அறிவேன். மேலும் அவ்வாறு விலகுவதால் எனது மருத்துவ சிகிச்சையும் எனது சட்ட ரீதியான உரிமைகளும் பாதிக்கப்படாது என்பதை கேட்டறிந்தேன்.

iii) நான் இந்த ஆய்விலிருந்து விலகினாலும் தற்போதய ஆய்விற்க்கும், எதிர்காலத்தில் இது தொடர்பாக நடத்தப்படும் ஆராய்ச்சிகளுக்கும், எனது மருத்துவ பதிவேடுகளை இந்த ஆய்வின் விசாரணையாளர்கள் பார்க்க எனது அனுமதி தேவையில்லை என்று அறிந்துகொண்டேன்.

iv) அறிவியல் நோக்காத்திற்காக இந்த ஆய்வின் மூலம் எழும்முடிவுகளையும், தகவல்களையும் நான் தடை செய்ய மாட்டேன் என்று ஒப்புக்கொள்கிறேன்.

v) மேற்கூறிய ஆய்வில் பங்கேற்க்க நான் ஒப்புக்கொள்கிறேன் .

<u>ஆய்வு தள முகவரி</u>
செல்ல சிந்து .கு.ந
சமூக சுகாதார மற்றும் வளர்ச்சி துறை, கிருத்துவ மருத்துவ கல்லூரி, வேலூர், தமிழ் நாடு, இந்தியா - 632002.

அலைபேசி: 9994325172

கையொப்பம் (அல்லது பெருவிரல் ரேகை) பங்கேற்ப் பவரின் பெற்றோர்/ காப்பாளர்/ பாதுகாவலர்:

கையொப்பமிடுபவரின் பெயர்: ----------

கையொப்பம்:----------

(அ)
பெருவிரல் ரேகை

ஆய்வாளரின் பெயர் _____

ஆய்வாளரின் கையொப்பம் _____

தேதி _____

சாட்சிக்கையெழுத்து அல்லது கைநாட்டு _____

சாட்சியின் பெயர் மற்றும் முகவரி _____

தேதி_____

Annexure V: Assent form to participate in the EPIAS (Effect of Preterm birth on Intellectual Ability South India) study

Study site address:

Department of Community health and development/ Department of Child and adolescent psychiatry,

Christian Medical College,

Vellore, Tamil Nadu,

India – 632002.

Assent Form

Title of Study:

Effect of pre-term birth on Intellectual ability – A community based non-concurrent cohort study in South India.

Principal Investigator: Dr. Chella Sindhu KN

Introduction:

You are being requested to participate in this study to find out the effect of pre-term birth on intellectual ability. Since you have been identified as one of the pre-term children born between the years 2001 to 2005 you are eligible to participate in the study. It is well known through research that a significant number of pre-term born children encounter intellectual problems that go unidentified until a later stage, and hence we would like you to take some of the tests with us that will help identify any intellectual problems that you may encounter later in near future and hence we can guide you to the concerned department for further evaluation and help that may avoid a lot of difficulties that you may face in future.

Why are we doing this study?

We want to find out if pre-term born children do really encounter significant intellectual problems during their subsequent growth and development. Also if this is found to be true we intend to design a routine screening program in the future where all pre-term born children will have an assessment done as early as two years of age so that early help can be offered to them, thereby helping them lead an independent and a productive life in future.

What will happen during the study?

If you agree to participate in this study, you will have a screening test performed on you at CHAD (Department of Community Health And Development). Your transportation and food charges for the day will be taken care of by the hospital. If during screening you are found to be screen positive you will be referred to the Department of Child and Adolescent psychiatry for further evaluation and guidance.

If at any time you experience any problems or discomfort during the study, you or your parents/ guardian/ caretaker will be expected to report this to the doctor. You or your parents/ guardian/ caretaker can further report about your discomfort to the concerned doctor.

Are there good things and bad things about the study?

We do not expect any harm or discomfort to happen to you during the study. The good thing about the study is that it will help in early identification of problems that you may encounter in future and hence early help can be sought by you.

Who will know about what I did in the study?

The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

Can I decide if I want to be in the study?

Nobody will be angry or upset with you if you do not want to be in this study. We will talk to your parents/ legal guardian/ care taker about the study and you should talk to them about it too.

Assent:

I was present when_____ read this form and gave my verbal assent.

Name of the Patient Signature Date

Name of the person who obtained consent Signature Date

Annexure VI: Facsimile of Assent document - Tamil

ஒப்புதல் படிவம்

ஆய்வு தள முகவரி

சமூக சுகாதார மற்றும் வளர்ச்சி துறை/ குழந்தைகள் மற்றும் இளைஞர் மனநல துறை

கிருத்துவ மருத்துவ கல்லூரி,

வேலூர், தமிழ் நாடு, இந்தியா **- 632002.**

ஆய்வின் தலைப்பு: குறைமாதப்பிறப்பு , அறிவுத்திறன் மீது ஏற்படுத்தும் தாக்கம் -- தென் இந்தியாவில் நடத்தப்படும் சமூகக்குழும ஆய்வு.

தலைமை ஆய்வாளர்: **மரு. செல்ல சிந்து .கு.ந**

முன்னுரை:

குறைமாதபிறப்பின் விளைவால் ஏற்படும் மூளை வளர்ச்சிக் குறைபாடுகளை கண்டறியும் ஆய்வில் தங்களை பங்கேற்குமாறு கேட்டுக்கொள்ளப்படுகிறது. தாங்கள் 2001 - 2005 வருடகலத்தில் குறைமாதத்தில் பிறந்த குழந்தைகளில் ஒருவரென்று கண்டறியப்பட்டதால் தாங்கள் இவ்வாய்வில் பங்கேற்க தகுதியுள்ளவர். குறைமாதத்தில் பிறந்த குழந்தைகளுக்கு ஏற்படும் அறிவுக் குறைபாடு நீண்டகாலம் கண்டறியப்படாமல் போவதாக ஆராய்ச்சிகள் பறைசாற்றுகின்றன. தங்களுக்கு எதிர்கலத்தில் ஏற்படும் அறிவுக்குறைபாடுகளை கண்டறிய எங்களுடைய சில சோதனைகளை ஏற்குமாறு வேண்டிக்கொள்கிறோம். இதன்முலம் கண்டறியப்பட்ட குறைபாட்டிற்கினங்க சம்மந்தபட்ட துறைஇலாகாவிற்கு அனுப்பப்பட்டு மேலும் பரிசோதிக்கப்பட்டு தேவையான உதவி வழங்கப்படும். பிற்காலத்தில் தாங்கள் எதிர்கொள்ளவேண்டிய பல இடர்கள் இதனால் தவிர்க்கப்படும்.

நாங்கள் ஏன் இந்த ஆய்வை மேற்கொள்கிறோம்?

குறைமாதத்தில் பிறந்த குழந்தைகளின் வளர்ச்சியின்போது உண்மையிலேயே அறிவுக்குறைபாடு ஏற்படுகிறதா என்று நாங்கள் கண்டறிய முனைந்துள்ளோம். ஒருகால் அது உண்மையென்று இந்த ஆய்வின்முலம் கண்டறியபட்டால், வருங்காலத்தில் இக்குறைபாட்டைக் கண்டறிய ஒரு மாதிரிசோதனை திட்டத்தை வழிவகுக்க எண்ணியுள்ளோம். இத்திட்டத்தின் மூலம் குறைமாதத்தில் பிறந்த குழந்தைகள் இரண்டு வயதிலேயே அறிவுவளர்ச்சி மதிப்பீடு செய்யப்பட்டு ஆரம்பகட்டத்திலேயே உதவி வழங்கப்படும். இதனால் அவர்களுடைய வாழ்க்கையை மற்றவர்களை சாராமல் சுதந்திரமாகவும், பயனுள்ளதாகவும் நடத்திச்செல்ல உதவமுடியும்.

இந்த ஆய்வின்போது என்ன செய்யப்படும்?

தாங்கள் இந்த ஆய்வில் பங்கேற்க சம்மதித்தால், தங்களுக்கு பரிசோதனை தேர்வு சமூக சுகாதார மற்றும் வளர்ச்சி துறையில் (CHAD) செய்யப்படும். அந்நாளுக்கான போக்குவரத்து

மற்றும் உணவு செலவுகள் மருத்துவமனையால் ஏற்கப்படும். அவ்வாறு பரிசோதிக்கும் பொழுது தங்களுக்கு குறைபாடு உள்ளது கண்டறியப்பட்டால், மேல்மதிப்பீடு மற்றும் வழிகாட்டுதலுக்காக குழந்தைகள் மற்றும் இளைஞர் மனநல துறைக்கு அனுப்பிவைக்கப்படுவீர்கள். தங்களுக்கு இந்த ஆய்வின் போது எந்தவித பிரச்சினையோ அசௌகரியமோ ஏற்பட்டால் தாங்களோ, தங்கள் பெற்றோர்/ காப்பாளர்/ பாதுகாவலரோ மருத்துவருக்கு உடன் தெரிவிக்குமாறு கேட்டுக்கொள்கிறோம். தாங்களோ தங்கள் பெற்றோர்/ காப்பாளர்/ பாதுகாவலரோ தங்களின் அசௌகரியம் பற்றி சம்பந்தப்பட்ட மருத்துவருக்கு தெரிவிக்கவும்.

இந்த ஆய்வை பற்றி நல்ல விஷயங்கள் மற்றும் கெட்ட விஷயங்கள் உள்ளதா?

தங்களுக்கு இந்த ஆய்வின்போது எந்தவித அசௌகரியமோ தீங்கோ ஏற்படாது என்று எதிர்பார்க்கிறோம். இந்த ஆய்வின் நல்ல விஷயம், தாங்கள் வருங்காலத்தில் எதிர்கொள்ளவிருக்கும் இடர்களை முன்பாகவே கண்டறியப்படுவதால் அறிவாற்றல் குறைபாட்டை அரம்ப காலத்திலேயே கண்டறிந்து மருத்துவ உதவியை தாங்கள் நாட முடியும்.

இந்த ஆய்வில் நான் என்ன செய்தேனென்று யாருக்கு தெரியும்?

இந்த ஆய்வின் முடிவுகள் ஒரு மருத்துவ இதழில் வெளியிடப்படும், ஆனால் தங்களுடைய பெயர், அடையாளம் மருத்துவ இதழ்களிலோ, விளக்கக் காட்சிகளிலோ வெளிவராது காக்கப்படும். இந்த ஆய்வில் நீங்கள் பங்கேற்க முடிவுசெய்தால், தங்களுடைய கூடுதல் அனுமதியின்றி தங்களின் மருத்துவ குறிப்புகள் இந்த ஆய்வில் சம்மந்தப்பட்டவர்களால் பரிசீலனை செய்யப்படும்.

இந்த ஆய்வில் பங்கேற்பதைப்பற்றி நான் முடிவு செய்ய முடியுமா?

தாங்கள் இந்த ஆய்வில் பங்கேற்காமல் விலகினால் யாரும் வருத்தமோ கோபமோ கொள்ளமாட்டார்கள். தங்களுடைய பெற்றோர்/ காப்பாளர்/ பாதுகாவலரிடம் இந்த ஆய்வு பற்றி நங்கள் விளக்குவோம். தாங்களும் அவர்களிடம் இதைப்பற்றி பேசித்தெரிந்து கொள்ளுமாறு கேட்டுக் கொள்கிறோம்.

<u>சம்மதம் தெரிவித்தல்:</u>

---------- இந்தப்படிவத்தை படிக்கும் பொழுது நான் இருந்து எனது வாய்மொழி ஒப்புதலை அளித்தேன்.

<u>ஆய்வுசெய்யபடுபவரின் பெயர் கையொப்பம் தேதி</u>

<u>ஒப்புதலை வாங்கியவரின் பெயர் கையொப்பம் தேதி</u>

Annexure VII: Institutional Review Board and Ethics committee approval for the research study

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA.

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Alfred Job Daniel, D Ortho, MS Ortho, DNB Ortho
Chairperson, Research Committee & Principal

Dr. Nihal Thomas,
MD., MNAMS., DNB (Endo), FRACP (Endo), FRCP (Glas) (EDIN)
Deputy Chairperson
Secretary, Ethics Committee, IRB
Additional Vice Principal (Research)

April 29, 2014

Dr. Chella Sindhu K. N
PG Registrar
Department of Community Health
Christian Medical College,
Vellore 632 002

Sub: **Fluid Research grant project:**
Effect of pre-term birth on Intellectual Ability - A community based non-concurrent cohort study in South India.
Dr. Chella Sindhu K. N, PG Registrar, Community Health, Dr. Kuryan George, Community Health, Dr. Paul Russell, Child and Adolescent Psychiatry Unit, Psychiatry.

Ref: IRB Min No. 8655 [OBSERVE] dated 19.02.2014

Dear Dr. Chella Sindhu K. N.

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "Effect of pre-term birth on Intellectual Ability - A community based non-concurrent cohort study in South India." on February 19, 2014.

The Committees reviewed the following documents:

1. IRB Application format
2. Curriculum Vitae' of Drs. Chella Sindhu K. N, Kuryan George, Paul Russell.
3. Informed Consent form (English &Tamil)
4. Information sheet (English & Tamil)
5. Assent form (English & Tamil)
6. No of documents 1-5

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002.
Tel : 0416 - 2284294, 2284202 Fax : 0416 - 2262788, 2284481 E-mail : research@cmcvellore.ac.in

Annexure VIII: Anti-plagiarism Certificate